DOES NOT CIRCULATE

Vol. 16 No. 2 Abstr. 292-590

August, 1954

UNIVERSITY OF MICHIGAN
SEP - 8 1954
MEDICAL LIBRARY

ABSTRACTS OF WORLD MEDICINE

A Monthly Critical Survey
of Periodicals in
Medicine and its Allied Sciences

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

Copyright

YEARLY SUBSCRIPTION £4.4.0 U.S.A. AND CANADA $13.50 SINGLE NUMBER 8/6

ABSTRACTS OF WORLD MEDICINE

UNDER THE DIRECTION OF

HUGH CLEGG, M.A., M.D., F.R.C.P., Editor, *BRITISH MEDICAL JOURNAL*

EDITOR

DONALD CROWTHER, B.A., B.M., B.Ch.

ASSISTANT EDITOR

A. DEWAR DUFF, M.B., Ch.B.

SUB-EDITOR

MARJORIE H. HOLLOWELL

This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals* and in *World Medical Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together under the same heading. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

Copyright 1954 by the British Medical Association

CONTENTS

[For Subject Index see end of text]

Correct vitamin balance for all ages

From the youngest to the oldest the routine administration of ABIDEC® ensures an adequate intake of vitamins in well-balanced proportions.

For infants and children Abidec **DROPS** are the ideal supplementary multivitamin treatment. For adults Abidec **CAPSULES** are invaluable in correcting suspected deficiencies due to bad dietary habits.

ABIDEC

® *Registered Trade Mark*

Abidec Drops are easily administered to infants and children, in food, a single daily dose being adequate. For adults, adequate intake is obtained with **ONE** *Abidec Capsule Daily.*

Parke, Davis & Company, Limited (*Inc. U.S.A.*) Hounslow, Middlesex. Tel: Hounslow 2361

63

ABSTRACTS OF WORLD MEDICINE

VOL. 16 NO. 2 AUGUST, 1954

Pathology

EXPERIMENTAL PATHOLOGY

292. **Intravascular Aggregation and Adhesiveness of the Blood Elements Associated with Alimentary Lipemia and Injections of Large Molecular Substances. Effect on Blood–Brain Barrier**

C. F. CULLEN and R. L. SWANK. *Circulation* [*Circulation (N.Y.)*] **9**, 335–346, March, 1954. 5 figs., 48 refs.

An investigation was carried out at McGill University, Montreal, into the effect of a high fat meal on the intact circulation of the hamster. A meal rich in fat (35% cream) was given by stomach tube to 35 hamsters, which were afterwards anaesthetized with 20% urethane intraperitoneally. One cheek pouch was then inverted and immersed in Ringer's solution at 37·5° C. to permit microscopical examination of the smaller blood vessels for several hours. Chylomicron, leucocyte, and platelet counts were determined on samples of blood from the femoral vein. Increased adhesiveness and aggregation of erythrocytes, which were covered by an adhesive film, were observed when the lipaemia had passed its peak; in some instances there was also clumping of platelets. These changes, which were accompanied by marked slowing of the circulation, were also observed in 22 hamsters given an intravenous injection of gelatin or dextran—that is, of substances of high molecular weight. In the latter group increased permeability of the blood vessels of the brain was demonstrated by intravenous injection of a saturated solution of trypan blue. From all these observations, the authors are prompted to suggest that a high-fat diet may be important in the pathogenesis of multiple sclerosis and vascular thrombosis. *A. Wynn Williams*

293. **The Role of the Bronchial Artery Circulation in the Etiology of Pulmonary and Pericardial Suppuration. An Experimental Study**

R. S. HAHN, E. HOLMAN, and J. B. FRERICHS. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 121–129, Feb., 1954. 7 figs., 28 refs.

A number of experiments were carried out at Stanford University School of Medicine, San Francisco, to determine the part played by the bronchial arterial circulation in infections of the lung. The introduction of multiple septic emboli into the right posterior bronchial artery of the dog failed to cause pulmonary infarction, suppuration, or abscess formation. There was, however, a high incidence of septic lesions in the mediastinal organs, pleura, pericardium, and myocardium. In further experiments injection of indian ink into the bronchial artery confirmed that it is in communication with the pericardium and myocardium. It is therefore suggested that further attention should be paid to the possible role of the bronchial artery in the transfer of infection to the pericardium and myocardium. *G. J. Cunningham*

294. **The Relation of Serum Stability to the Development of Arteriosclerosis**

N. RESSLER, A. J. BOYLE, and M. KOSAI. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 194–200, Feb., 1954. 8 refs.

In an investigation carried out at Wayne University, Detroit, into the possible relation of arteriosclerotic changes to diminished colloid stability in the serum, various metallic ions were added to serum from patients with arteriosclerosis and other diseases and the degree of turbidity which developed was estimated with a spectrophotometer. Taking the light transmission of serum before the addition of the metallic salt as 100%, the fall in transmission when measured at a standard interval after the addition of the salt provides a measure of the increase in turbidity due to disturbance of the colloid state. With serum from normal control subjects the average values after the addition of salts of manganese, nickel, copper, and zinc were 79%, 89·3%, 111·1%, and 106% respectively. With serum from arteriosclerotic patients the transmission after addition of each ion was less than the normal figure in 90% of cases, indicating diminished serum colloid stability.

The various factors influencing colloid stability are discussed. The authors suggest that as the blood transudate passes through the arterial wall the elastin competes with the plasma proteins for cations such as calcium, and this may effect the dispersion of less soluble components of the plasma, such as cholesterol, and lead to their precipitation. *Peter Harvey*

295. **Gastrointestinal Function in Experimental Hepatic Insufficiency**

P. C. REYNELL. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **35**, 92–95, Feb., 1954. 2 figs., 6 refs.

An investigation was carried out in the Nuffield Department of Clinical Medicine, Oxford, to determine whether the gastrointestinal symptoms commonly observed in viral hepatitis are due to changes in the upper intestinal tract or to some other, toxic, factor. Acute hepatic insufficiency was produced in two groups

of rats by injection of carbon tetrachloride and subtotal hepatectomy respectively. In both groups there was marked anorexia, and radiographs revealed considerable delay in gastric emptying. These changes were not noted in the animals after division of the bile duct, vagotomy, or administration of hexamethonium bromide.

It is considered, therefore, that the nausea, anorexia, and vomiting which occur in acute hepatitis are due to some humoral process following hepatic damage, and not to concurrent gastroduodenitis. *J. B. Wilson*

CHEMICAL PATHOLOGY

296. **Acid-phosphatase Activity of Normal and Neoplastic Human Tissues**

H. M. LEMON, M. M. DAVISON, and I. ASIMOV. *Cancer* [*Cancer* (*N.Y.*)] **7**, 92–99, Jan., 1954. 5 figs., bibliography.

The acid phosphatases are the only enzymes which frequently show increased activity in the serum of patients with cancer. Although the estimation of this increase has been of greatest value in the diagnosis of cancer of the prostate with bony metastases, increased phosphatase activity is known to be also present in patients with metastatic adenocarcinoma from other sites, such as the breast, thyroid gland, or colon, extensively invading bone. Since little is known of the origin of increased acid-phosphatase activity in such cases of non-prostatic origin, the authors, at the Boston University School of Medicine, have compared the relative acid-phosphatase activity in normal and neoplastic human tissues by determining the rate of hydrolysis of glycerophosphate and phenylphosphate esters in serial-section aliquots of neoplastic and homologous normal tissues; their method of correcting this to a "per cell" basis by estimating the deoxypentose and nitrogen content of each tissue sample is described.

The tissue concentration of acid phosphatase in benign tumours and inflammatory lesions was found to be essentially the same as in normal tissues. Adenocarcinoma of the colon, however, showed a significant increase in tissue acid-phosphatase content over that of adjacent normal tissue from the colon. An increase was also found in other types of adenocarcinoma and in some epidermoid and sarcomatous tumours compared with homologous normal tissue. The authors suggest that this increase in the acid-phosphatase content of cancerous tissues may be one factor contributing to the increased serum acid-phosphatase activity in patients with metastatic tumours. *L. A. Elson*

297. **The Bromsulphthalein-retention Test in Acute Cholecystitis and in Some Other Acute Intra-abdominal Conditions**

W. BURNETT. *Lancet* [*Lancet*] **1**, 488–490, March 6, 1954. 2 figs., 6 refs.

The "bromsulphalein" retention test of liver function was used at Aberdeen Royal Infirmary in 46 cases of gall-bladder disease and 32 of acute non-biliary intraperitoneal infection. Retention of the dye was observed in 22 of 23 cases of acute cholecystitis, the degree of retention being greater in cases showing the most inflammatory change in the gall-bladder. It is suggested that the results of this test may be helpful in deciding whether the initial treatment of acute cholecystitis should be conservative or surgical. The results were negative in the remaining 23 cases of gall-bladder disease in which there was no acute inflammation; these included 20 cases of chronic cholecystitis, 2 cases of biliary colic with a stone impacted in the neck of the gall-bladder, and one case of volvulus of the gall-bladder with infarction. A positive result was obtained in only 5 of the 32 cases of acute intra-abdominal conditions other than biliary disease, which included 16 cases of acute appendicitis and 9 of perforated peptic ulcer. Of these 5 positive results, 3 were associated with severe peritonitis and one with intraperitoneal haemorrhage. The subcutaneous injection of morphine resulted in a steep rise in pressure in the bile duct, and the author suggests that the bromsulphalein test should not be performed after morphine has been given. In 6 patients the test was negative before, and positive after, the injection of 1/6 gr. (11 mg.) of morphine. *M. J. H. Smith*

298. **Chemical Assay of Gonadotrophin in Urine**

A. C. CROOKE, W. R. BUTT, J. D. INGRAM, and L. E. ROMANCHUCK. *Lancet* [*Lancet*] **1**, 379–383, Feb. 20, 1954. 4 figs., 16 refs.

The two first-named authors have previously shown by means of column chromatography that urine contains two gonadotrophic substances, gonadotrophin A and gonadotrophin B. In the present paper from the United Birmingham Hospitals the authors describe a chemical method for the assay of gonadotrophin A, which occurs in high concentration in the urine of postmenopausal women and in that of all women during certain phases of the menstrual cycle. Gonadotrophin A is absorbed as a sharp brown band on a column of tricalcium phosphate and eluted in a fairly pure state by 0·002 M disodium hydrogen phosphate; its different components can be estimated in the eluate by non-specific reactions, the ninhydrin reaction being employed for free amino groups, the orcinol reaction for hexose, and the polarographic method for proteins. A second, more diffuse, brown band in the chromatogram represents the group of substances known as gonadotrophin B, which can be eluted with 0·02 M tribasic sodium phosphate; it occurs in high concentration in the urine of pregnant women, but in the present study no attempt was made to estimate it quantitatively.

The method is briefly as follows. Gonadotrophin A is extracted from 100 ml. of urine by absorption on kaolin or benzoic acid and purified either (1) by chromatography on columns of tricalcium phosphate or (2) by dissolving the kaolin extract in disodium phosphate and extracting impurities by shaking with tricalcium phosphate (this second, shorter method, though not as accurate as column chromatography, is adequate for routine work). Physico-chemical investigations showed that gonadotrophin A is a fairly pure protein, and in biological tests it was confirmed that gonadotrophin A prepared by

column chromatography has follicle-stimulating but not luteinizing properties.

Urine from 5 healthy women was assayed at short intervals during 6 menstrual cycles. The average minimum level of excretion of gonadotrophin A was 25 μg. per hour (range 15 to 60 μg.) and the average maximum 203 μg. (range 120 to 300 μg.). In general, one peak occurred during the follicular phase of the cycle and one during the luteal phase. In women with amenorrhoea of unknown origin the excretion of gonadotrophin A was quite irregular and sometimes increased erratically to very high levels. The excretion in men and in children was within the range found in normally menstruating women. *Nancy Gough*

HAEMATOLOGY

299. **An Action of Thrombin on Platelets in Accelerating Clotting**
J. F. DESFORGES and F. S. BIGELOW. *Blood* [*Blood*] **9**, 153–162, Feb., 1954. 3 figs., 21 refs.

A series of experiments designed to show that thrombin will enhance the thromboplastic activity of platelets in the presence of calcium was carried out at the Boston City Hospital (Harvard Medical School). Thrombin-treated platelets were obtained by incubating a suspension of platelets in an equal volume of bovine thrombin at room temperature for 30 minutes; when human thrombin was used the platelet suspension was incubated for several hours. The platelets were subsequently thoroughly washed.

The addition of treated platelets to haemophilic and normal blood accelerated the clotting time to a greater extent than the addition of control platelets. When treated platelets were added to normal or haemophilic plasma the recalcification time was considerably shortened. In order to exclude the possibility that these effects were due to the direct action of traces of thrombin upon fibrinogen, prothrombin consumption and thrombin production were studied, treated platelets being substituted for thromboplastin. The results showed that the thromboplastic activity of platelets treated with thrombin was enhanced. Thrombin solutions without platelets and thrombin-treated erythrocytes did not accelerate prothrombin conversion when substituted for thromboplastin.

The phenomenon of clumping and disintegration of platelets was observed in only a few of the experiments, its occurrence being unrelated to the degree of thromboplastic activity manifested. *Nigel Compston*

300. **Differentiation of Plasma Antithrombin Activities**
C. FELL, N. IVANOVIC, S. A. JOHNSON, and W. H. SEEGERS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 199–202, Feb., 1954. 9 refs.

It has been suggested that there are four types of antithrombin activity: the ability of fibrin to adsorb thrombin (I); the plasma co-factor of heparin (II), which with heparin interferes with the action of thrombin on fibrinogen; (III) a plasma antithrombin activity distinct from II and unrelated to heparin; and a plasma factor (IV) which interferes with the formation of thrombin from prothrombin, but which has no action on purified preformed thrombin. The last-named antithrombin activity (IV) has been demonstrated only in ether-treated plasma which is free from antithrombin III. In the study here reported from Wayne University School of Medicine, Detroit, certain properties of antithrombin activities II, III, and IV were investigated and the results compared with those of a factor which appears to act with heparin on the conversion of prothrombin to thrombin; this factor the authors call the " '39 factor ", since it was discovered in 1939 by Brinkhous *et al.* (*Amer. J. Physiol.*, 1939, **125**, 683), but has received no attention since then.

All four antithrombin factors are water-soluble and are destroyed by heating at 70° C., but not at 60° C., for 3 minutes. They are not absorbed on barium carbonate, and only antithrombin III is removed by ether treatment of plasma. On ammonium sulphate fractionation of fresh bovine plasma at 50% and 70% of saturation, antithrombin factor II was found chiefly in the 50 to 70% fraction, and factor III only in the 0 to 50% fraction. Factors II and III thus appear to be distinct entities. Fractionation results in respect of IV were inconclusive, and the relation of IV to II and III is not clear. The behaviour of '39 factor closely resembled that of antithrombin II. *A. Brown*

301. **The Total Circulating Eosinophil Count under Environmental and Stress Stimuli**
E. NAIDEN and S. ROSS. *Journal of Pediatrics* [*J. Pediat.*] **44**, 145–152, Feb., 1954. 29 refs.

MORBID ANATOMY AND CYTOLOGY

302. **The Pathogenesis of Non-specific and Rheumatic Bursitis.** (Zur Pathogenese der unspezifischen und rheumatischen Schleimbeutelentzündungen)
R. BÖHMIG. *Zentralblatt für allgemeine Pathologie und pathologische Anatomie* [*Zbl. allg. Path. path. Anat.*] **91**, 245–252, Feb. 22, 1954. 3 figs., 16 refs.

Examination at the City Pathological Institute, Karlsruhe, of 30 excised bursae, 21 of which were diagnosed as examples of non-specific and 9 of rheumatic bursitis, showed the following changes.

(1) *Serous inflammation.* This lesion was most pronounced in acute bursitis, and is therefore seldom examined histologically. The protein-containing exudate occurs under the endothelial lining of the bursa, but may also separate the atrophied collagen fibres below it. These fibres may show small groups of cells with pyknotic nuclei, loss of chromatin and staining, and even reduction of the nuclei to nuclear shadows.

(2) *Fibrinous inflammation.* This was found to be present in all subacute and subchronic cases. The fibrin is laid down in layers immediately under the endothelial lining of the bursa and between the deeper collagen fibres. Villous projections develop from the endothelial

surface into the lumen; they are covered with endothelium and filled with hyalinized material, larger or smaller amounts of fibrin, and elastic fibres or relics of them.

(3) *Haemorrhages and cellular infiltration.* In this series both these findings were rare. When cellular infiltration occurs it is mainly into the middle and outer wall of the bursa.

(4) *Formation of new vessels.* The author distinguishes between the vascular structures developing from arterioles in the middle wall and the new capillaries which develop in the inner wall, often in association with villous projections.

(5) *Histiocytic proliferation.* This appeared to occur during fibrinous inflammation, and developed either in the subendothelial layer (particularly in the fibrinous centres of the villi) or in the intercollagenous bands of fibrin. Palisading of histiocytes may occur to replace the endothelium, in whole or in part, or to cover the outer layers of fibrin; it is always associated with formation of new capillaries.

The author considers that the association of interstitial fibrinous inflammation, histiocytic proliferation, and formation of new capillaries is characteristic of rheumatism, and compares bursitis fibrinosa simplex (which does not possess all these characters) with non-specific fibrinous endocarditis, and also rheumatic fibrinous bursitis with rheumatic endocarditis. *C. L. Oakley*

303. **The Brain-stem Lesions in Parkinsonism**

J. G. GREENFIELD and F. D. BOSANQUET. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **16**, 213–226, Nov., 1953. 15 figs., 30 refs.

In briefly discussing the main contributions to the literature of Parkinsonism, the authors comment on the curious fact that no author writing in the English language mentions the characteristic types of cell degeneration occasionally found in the brain stem in this disease, although they were described by Lewy as long ago as 1912. The study now reported, which was carried out at the National Hospital, Queen Square, London, and the Radcliffe Infirmary, Oxford, was based on 19 cases of idiopathic paralysis agitans, 10 cases of Parkinsonism with a history of encephalitis lethargica, and 5 atypical cases of Parkinsonism; for purposes of comparison, 19 control cases with evidence of disease of the central nervous system, but not of Parkinsonism, were also examined.

The following five distinct types of cell change were identified in the substantia nigra and locus caeruleus. (1) An accumulation of lipochrome granules in the cells, accompanied by distension of the cell and disappearance of the nucleus and melanin granules. (2) Vacuolation of the cells—but this was an infrequent occurrence. (3) The presence of binucleated nerve cells; these were seen in the substantia nigra in 3 of the post-encephalitic cases and in the nucleus pontis in one case of idiopathic paralysis agitans. (The authors do not consider these first three lesions to be characteristic of Parkinsonism.) (4) The occurrence in the brain-stem cells of the spherical hyaline inclusion bodies first described by Trétiakoff in 1919 and named by him " Lewy bodies ". These oval or spherical bodies lie in the cytoplasm, usually among the melanin granules, but may be seen in cells with little or no pigment. (A table giving the reactions of these bodies to some 20 different stains is included in the text, as well as two excellent coloured photomicrographs depicting their appearance.) These inclusion bodies were present in all cases of typical idiopathic paralysis agitans and in one case of Parkinsonism which was probably post-encephalitic. (5) Neurofibrillary tangles, which were rather similar to those found in Alzheimer's disease but were not accompanied by senile plaques, were found in 9 post-encephalitic cases, in one case with amyotrophy, and in one of the cases of idiopathic paralysis agitans.

The interpretation of these cell changes is given in the form of answers to three questions: (1) Do these lesions occur as one of the processes of senility in an abnormal situation? The authors reject this interpretation, because the type of cell degeneration exhibiting Lewy's inclusions is not a usual finding in senility. (2) Are these changes in idiopathic paralysis agitans specific for this disease, or characteristic of it? While the authors do not claim that the changes are specific—since they have been found, though rarely, in other diseases—they believe that the combination of loss of certain cell groups in the substantia nigra with the presence of numerous Lewy's inclusion bodies in the pigmented cells is certainly characteristic of this disease. (3) Are the differences between the lesions of idiopathic paralysis agitans and post-encephalitic Parkinsonism qualitative or merely quantitative? The authors do not draw a sharp qualitative distinction between the two diseases. They suggest that the final answer to these questions must await the results of examination of a much larger series of cases of Parkinsonism with particular attention to the lesions in the pigmented cells of the midbrain and pons.

Ruby O. Stern

304. **A Histological and Chemical Study of Three Cases of Diffuse Cerebral Sclerosis**

W. BLACKWOOD and J. N. CUMINGS. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 33–49, Feb., 1954. 34 figs., 28 refs.

305. **Pathological Observations on Tuberculous Meningitis, before and since Streptomycin**

A. R. MACGREGOR. *Edinburgh Medical Journal* [*Edinb. med. J.*] **61**, 33–36, Feb., 1954. 4 figs., 2 refs.

The author describes the great improvement that has taken place in recent years in the prognosis of tuberculous meningitis in children, recalling from her personal experience that in the 14 years ending in 1951, of all patients coming to necropsy at a general children's hospital, 12·5% had died of tuberculosis, and 80% of these of tuberculous meningitis, among the 259 cases of which there were no survivors. Since the advent of streptomycin the situation has greatly improved, but there are still too many failures. The causes of failure of treatment are considered under three main headings.

(1) Failure to eliminate the infection; this may be due to (*a*) inaccessibility of the bacilli to the drug, or (*b*) to the development of drug resistance in the bacilli. Inaccessibility is most frequently a result of the bacilli being embedded in a dense fibrinous exudate, and a further complication is the formation of avascular caseous masses in the meningeal exudate, which are difficult to liquefy and, persisting, may act as sources of re-infection. (2) The second main cause of failure is hydrocephalus, which arises from the obstruction caused by the exudate in the subarachnoid space; usually mild at first, it may later be accentuated by further blockage due to fibrotic organization of the exudate to a degree such as to preclude all chance of full recovery. (3) Lesions in the brain substance; these may take one of two forms (*a*) tuberculous meningo-encephalitis, or (*b*) vascular changes resulting in areas of softening of the brain tissue and due to the gross fibrous intimal thickening of the arteries caused by acute or chronic tuberculous endarteritis.

The author's main conclusion is that success in treatment of tuberculous meningitis, perhaps more than in any other disease, depends on early diagnosis and early institution of effective treatment. *R. Heptinstall*

306. **Pathology of Chronic Bronchitis**
L. McA. Reid. *Lancet* [*Lancet*] **1**, 275–278, Feb. 6, 1954. 14 figs., 3 refs.

An attempt is here made to correlate the histology of the lung in chronic bronchitis with the natural history of the disease. At the Brompton Hospital, London, portions of lung were obtained at necropsy (16 cases) or at operation (8 cases) from patients who had had chronic bronchitis. Specimens of the bronchial mucosa taken at bronchoscopy in 6 cases were also examined histologically. From 10 of the lung specimens obtained at necropsy, 14 blocks were sectioned serially. In early cases changes were most marked in the bronchi, these being hypertrophy of the mucus-secreting elements, with an obvious increase in the number of goblet cells and dilatation of the ducts of the hypertrophied mucous glands. In advanced cases the bronchioles were severely affected, the changes including purulent bronchiolitis, bronchiolar abscesses, narrowing, obliteration, and dilatation. Alveolar changes—pneumonia, collapse, and emphysema—are considered to be largely the result of these disorders of the bronchioles. The author states that the principal abnormality in the early phase appears to be an excess of mucus in the respiratory tract. The appearances at necropsy are the result of recurrent acute inflammation, the scarring which may result from healing, and the compensatory changes induced. In many cases showing acute changes the functional disturbance may be temporary, but in others it is irreversible and permanent. Though each clinical attack may have little immediate effect, the cumulative action of several attacks may be great, since the most severe damage occurs in the bronchioles, where small changes can cause considerable functional disability.

[There are some excellent colour photomicrographs of the principal histological changes.] *J. R. Bignall*

307. **Observations on Interstitial Pneumonia in Infancy.** (Beobachtungen bei interstitieller Pneumonie im Säuglingsalter)
E. Fasske, H. König, W. Plettenberg, and H. U. Sauerbrei. *Zentralblatt für allgemeine Pathologie und pathologische Anatomie* [*Zbl. allg. Path. path. Anat.*] **91**, 267–279, Feb. 22, 1954. 11 figs., 31 refs.

The authors report, from the Municipal Children's Clinic, Essen, 33 cases of interstitial pneumonia in premature or feeble newborn children (16 boys, 17 girls), of whom 4 boys and 11 girls died. The birth weight of 14 of the 15 infants who died was between 1,500 and 2,000 g. The administration of chloramphenicol, oxytetracycline both parenterally and by aerosol, ACTH, " cyren-B ", gamma globulin, rutin, vitamin A (300,000 units), and vitamin D was without any certain therapeutic effect; nor had cyren-B, antibiotics, or rutin any prophylactic effect, even when the rutin was given 14 to 26 days before the outbreak of interstitial pneumonia. In 9 of the children there was a marked pleocytosis in the cerebrospinal fluid.

At post-mortem examination, carried out on 14 children, the diagnosis was confirmed in all cases, *Pneumocystis carinii* being demonstrated in the lungs of 11. The lungs showed thickening of all lobes, with compensatory emphysema but without pleural involvement. The septa were thickened, and reddish opalescent fluid could be expressed; the hilar lymph nodes were only slightly enlarged. Histological examination of the lung showed thickening and dense infiltration of the septa with histiocytes and relatively small numbers of plasma cells. (The patients who survived longer showed early fibrosis of the septa.) There was also shedding of the alveolar epithelium, which showed fatty changes. The alveoli contained both honey-comb and cystic forms of *P. carinii* in a small amount of free oedema fluid. The organism could not be demonstrated in any other organ, and attempts to infect mice and guinea-pigs with it failed.

The authors consider it very likely that *P. carinii* is the cause of some cases of infantile interstitial pneumonia. *C. L. Oakley*

308. **Endogenous Lipoid Pneumonia with Special Reference to Carcinoma of the Lung**
S. De Navasquez and G. A. D. Haslewood. *Thorax* [*Thorax*] **9**, 35–37, March, 1954. 2 figs., 2 refs.

The authors, working at Guy's Hospital, London, have carried out a histological and chemical investigation into the incidence and pathogenesis of endogenous lipoid pneumonia in lungs obtained at necropsy in 42 cases of a wide variety of pulmonary diseases. Histologically demonstrable fat was absent from the lung in cases of acute infection, but present in all cases of chronic infection and carcinoma examined. In the necrotic areas of tumours and in caseous tuberculous foci the fat was extracellular; elsewhere it was mainly found in intra-alveolar macrophages.

In 9 cases of carcinoma of the lung the total fat content of tumour tissue was determined by ether extraction of dried tissue samples. Tumour tissue contained significantly more extractable fat than normal tissue from the

opposite lung (13·09 and 8·63 g. per 100 g. dry tissue respectively). In both tissues cholesterol formed about 20% of the total fat content. No correlation was found between the amount of fat seen in sections and the amount extracted with ether.

The authors conclude that fat is liberated during the process of cell degeneration caused by chronic infection or in tumours and is phagocytosed by macrophages, the local persistence of which may produce a picture similar to that of the "lipoid pneumonia" due to inhalation of oil.

[Since the amount of fat seen in a section depends considerably on the staining method used and the thickness of the section, it is unfortunate that no details are given regarding these points. Histochemical methods for demonstrating cholesterol do not appear to have been used.] *M. C. Berenbaum*

309. **Manifest and Concealed Extension of Pulmonary Carcinoma to the Contralateral Lung; an Anatomical, Radiological, and Histological Study.** (La diffusione manifesta e quella larvata del cancro del polmone al polmone controlaterale; ricerche sistematiche anatomo-radiologiche ed istologiche)
C. MARINO and F. BIANCHI. *Archivio "De Vecchi" per l'anatomia patologica e la medicina clinica* [*Arch. "De Vecchi" Anat. patol.*] **20**, 31–125, Nov., 1953. 25 figs., bibliography.

This extensive study of the spread to the opposite lung of primary pulmonary neoplasms is based on the findings in 37 cases of carcinoma of lung examined post mortem at the Pathological Institute of the University of Florence betwee 1945 and 1952. Specimens were taken systematically from all parts of the lungs, five different stains were used, and over 1,000 slides were examined. The results of this examination were correlated with the clinical history and the *x*-ray findings (except in 5 cases first diagnosed at necropsy) and are reported in detail.

There were 13 anaplastic carcinomata (35%), 14 adenocarcinomata (37%), 6 squamous carcinomata (16%), and 4 polymorphic-celled growths (12%). The ipsilateral lymph nodes and bronchial walls were involved in all cases, and in all but 9 cases there was evidence of direct or metastatic spread to the lymph nodes or into the pulmonary parenchyma on the opposite side, by the lymphatic route in 12 out of 34 cases (35%) and via the bronchi in 9 (27%). Free fragments of neoplastic tissue were observed in the alveoli and infundibula, mainly in the lower lobes, in 7 cases—mostly of squamous carcinoma—but only in 2 of these was there evidence of independent proliferation and invasion. Spread to the opposite lung by the blood stream was rare, occurring in 3 cases only. The importance of lymph-node involvement as a preliminary to infiltration of the parenchyma of the opposite lung is stressed repeatedly.

[The mechanism of spread of carcinoma of the lung to the opposite side has hitherto received comparatively little attention, and although the author cites 26 references in the literature to this aspect of the subject, only one previous systematic histological investigation appears to have been reported.] *Ferdinand Hillman*

310. **Bronchopulmonary Sarcoma**
L. IVERSON. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 130–148, Feb., 1954. 13 figs., bibliography.

A search of the literature for the period 1900 to 1950 revealed only 16 reported cases of pulmonary sarcoma; to this number the author adds 3 more taken from the records of the Armed Forces Institute of Pathology, Washington, D.C. In most of these 19 cases the tumour was slow-growing, metastasis being observed in only 6. Criteria for differentiating pulmonary sarcoma from endobronchial sarcoma are given. The latter is relatively less malignant than pulmonary sarcoma, and is found chiefly in young adults [though the number of such cases (8) hardly seems large enough to warrant this last statement]. Conditions which may simulate bronchopulmonary sarcoma are discussed, in particular inflammatory states and undifferentiated bronchogenic carcinoma. *G. J. Cunningham*

311. **Erythrophagocytosis and Hemosiderosis in Lymph Nodes, Spleen and Liver in Patients Dying of Malignant Hypertension, Chronic Glomerulonephritis and Pyelonephritis and Polycystic Disease**
E. E. MUIRHEAD and W. F. SHIELDS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **40**, 307–312, Feb., 1954. 4 figs., 7 refs.

The spleen, liver, and abdominal lymph nodes of 28 uraemic subjects were examined microscopically at the University of Texas. In 23 of them some combination of erythrophagocytosis, haemosiderosis, and haemorrhage into lymph sinuses was seen, the appearances resembling those found in experimental uraemia associated with haemolytic anaemia. Whether these changes in man are related to the pathogenesis of the anaemia of uraemia remains to be demonstrated.

J. B. Enticknap

312. **The Morbid Histology of Cutaneo-mucous Naevo-carcinomata.** (Histopathologie des nævo-carcinomes cutanéo-muqueux)
C. BIMES. *Bulletin de l'Association française pour l'étude du cancer* [*Bull. Ass. franç. Cancer*] **40**, 481–528, 1953. 32 figs., bibliography.

Basing his conclusions on a review of the recent literature of cutaneo-mucous naevo-carcinoma and particularly on the histological study of 120 cases seen at the Centre Anticancéreux, Toulouse, and of 40 personal cases seen in private practice, the author presents a detailed description of the origin, histology, and diagnosis of these tumours. He has found Champy's osmium iodide method of fixation for the cells of the adrenal medulla to give also excellent impregnation of melanoblasts and malignant melanoma cells, a fact which he considers provides additional evidence for the common origin of all three.

[Justice cannot be done to this excellent and well illustrated general account in a short abstract, and the paper should be read in the original. It is of especial interest for its examination, whole-hearted acceptance, and application of Masson's view of the neural origin of the melanoblast.] *Bernard Lennox*

Bacteriology

313. **Immunization of Young Babies against Diphtheria**
N. R. BUTLER, M. BARR, and A. T. GLENNY. *British Medical Journal* [*Brit. med. J.*] **1**, 476–481, Feb. 27, 1954. 3 figs., 12 refs.

An effective method of immunizing babies against diphtheria at an earlier age than has hitherto been recommended would be of value in the maintenance of a high level of immunity in the child population. While the eagerness of mothers to have their children immunized against diphtheria has noticeably flagged with the virtual disappearance of that disease, most mothers are anxious to have them immunized against whooping-cough, so that the opportunity arises for immunization against diphtheria at the same time. However, whooping-cough immunization should be carried out as early in life as possible, and while it has been shown that immunization against the two diseases can be successfully combined at a later age, the question arises whether immunization against diphtheria started during the first two weeks of life is likely to be effective in the presence of a high serum titre of inherited antitoxin, which may neutralize some or all of the injected prophylactic. Barr *et al.* have shown previously that babies of 6 to 10 days in whose serum the level of diphtheria antitoxin had fallen below 0·04 unit per ml. could be successfully immunized with A.P.T. (*Lancet*, 1952, **2**, 803; *Abstracts of World Medicine*, 1953, **13**, 272), but in babies with higher serum antitoxin levels the response was less satisfactory. To overcome this difficulty, Bousfield (*Lancet*, 1951, **1**, 1028; *Abstracts of World Medicine*, 1951, **10**, 490) proposed the use of a preparation (F.P.T.) containing free fluid toxoid in addition to absorbed toxoid, the former being intended to combine rapidly with the circulating antitoxin, leaving the precipitated toxoid free to exert its immunizing stimulus without interference.

The present work is concerned with the serum antitoxin titres obtained in 180 newborn babies after immunization at University College Hospital, London, with F.P.T. combined with pertussis vaccine. Two injections of F.P.T. were given, the interval being 6 weeks in some cases and 14 weeks in others, and serum antitoxin levels were determined 8 weeks and 12 weeks respectively after the second injection. The results again confirmed that an existing high level of passively conferred antitoxin interferes with the active production of antitoxin by immunization, and that the use of F.P.T. does not reduce this interference appreciably. Babies with a serum antitoxin titre below 1 unit per ml. gave a better response if injected at 1 week and 14 weeks of age than if injected at 1 week and 6 weeks, whereas if the titre of the cord blood was more than 1 unit per ml. the shorter interval between injections produced the better response. A few babies with a low titre in the cord blood responded better to P.T.A.P. than did comparable babies to F.P.T. F.P.T. gave rise to few general or local reactions.

K. S. Zinnemann

314. **Observations on the Histology of the Arthus Reaction and its Relation to Other Known Types of Skin Hypersensitivity**
P. G. H. GELL and I. T. HINDE. *International Archives of Allergy and Applied Immunology* [*Int. Arch. Allergy*] **5**, 23–46, 1954. 8 figs., 12 refs.

In a study carried out at the University of Birmingham the Arthus phenomenon—which consists in the development of haemorrhage and central necrosis in the skin of anaphylactically sensitized animals given successive skin tests with specific antigen—was produced in rabbits by weekly subcutaneous or intravenous injection of human plasma. Alum-precipitated human plasma or ovalbumen was also used. The Arthus reaction was investigated histologically at various stages from the 2nd hour to the 25th day after its appearance.

The authors show that in this reaction there are two stages, which can best be distinguished if necrosis is avoided or kept to a minimum. The first stage is a polymorphonuclear perivascular reaction. At 8 hours the polymorphs begin to degenerate, and from this moment onwards an increasing mononuclear infiltration —the second stage—becomes pronounced. Later on, immature plasma cells appear, and from the 3rd to the 6th day immature and mature plasma cells are numerous. This second mononuclear stage is not regarded as a repair reaction, and its similarity to the tuberculin-type reaction is stressed. When rabbits were passively sensitized with plasma the only reaction produced resembled that of the first stage of the Arthus reaction, but when sensitization was induced with leucocytes the second or mononuclear stage predominated, although full maturation to the plasma-cell stage did not occur. The authors suggest that the first stage of the Arthus phenomenon is equivalent to an immediate anaphylactic reaction, while the second stage is equivalent to the delayed type of reaction. The maturation to plasma cells is thought to be connected with the production of " free " antibody.

H. Herxheimer

315. **The Combined Actions of Chloramphenicol and of Bactericidal Antibody plus Complement on *Salmonella typhosa***
H. P. TREFFERS and L. H. MUSCHEL. *Journal of Experimental Medicine* [*J. exp. Med.*] **99**, 155–165, Feb. 1, 1954. 3 figs., 10 refs.

At Yale University, New Haven, Connecticut, the authors, using quantitative assay methods of some sensitivity, carried out a number of experiments to investigate the possible synergistic or antagonistic action between a bactericidal system (specific antibody and complement) and chloramphenicol. The test organism was *Salmonella typhosa* Ty 2, and the rabbit antiserum used contained both O- and Vi-antibodies. Joint, but independent, action (additive inhibitions) of the two groups of reagents was observed, their combined

activities being predicted within 3% from a knowledge of their separate activities. Four-fold increase in chloramphenicol resistance of the 0901 strain of *Salm. typhosa* had little if any effect on its susceptibility to the bactericidal action of O-antibody and complement.

Joyce Wright

316. **Immunogenicity Studies in Human Subjects of Trivalent Tissue Culture Poliomyelitis Vaccine Inactivated by Ultraviolet Irradiation**

A. MILZER, S. O. LEVINSON, H. J. SHAUGHNESSY, M. JANOTA, K. VANDERBOOM, and F. OPPENHEIMER. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 26–33, Jan., 1954. 32 refs.

The polyvalent vaccine employed in the studies here reported from the Michael Reese Research Foundation and Hospital, Chicago, was prepared from monkey kidney tissue culture, in a protein-free medium, of poliomyelitis virus strain Mahoney (for Type 1), strain M.E.F.-I (for Type 2), and Saukett (for Type 3). Each strain was grown individually, the virus in the culture fluid being then titrated and its identity cross-checked with a number of type-specific sera from different sources. All virus titrations and serum neutralization tests were carried out in roller-tube cultures of monkey kidney tissue. Before being inactivated by ultraviolet irradiation the pools of the individual culture types were tested for bacterial sterility and then centrifuged to remove tissue particles and other debris. The inactivation of the cultures was carried out in two centrifugal filmers of the Levinson–Oppenheimer-type connected in series, with a film thickness of 25 μ and a flow rate of 200 ml. per minute. The total exposure time was 2 seconds and the ultraviolet energy absorbed by the film was 4×10^{-6} Einstein per ml. Inactivation was confirmed by the following stringent tests: (1) repeated and combined intracerebral and intraperitoneal injections of the undiluted irradiated material into monkeys; (2) tissue-culture inoculations followed by subcultures; (3) photoreactivation; and (4) further tests for bacterial sterility.

The three type cultures were then pooled and the resulting trivalent vaccine emulsified in an equal part of a purified mineral-oil adjuvant. One ml. of the mixture was injected intramuscularly into 30 adult volunteers, this injection being followed one month later by another of 1 ml. of an aqueous trivalent vaccine (that is, without the oil adjuvant) also given intramuscularly. The local and general reactions to both vaccines were minimal. Blood was collected from each subject before inoculation and 2 weeks after the second injection. Before vaccination 63% of the subjects had measurable antibodies to all three types of virus, 27% to two types, and 10% to one type only. Post-vaccination determination of titres showed a fourfold or greater rise in titre in 63% for Type 1, 83% for Type 2, and 90% for Type 3. There was no evidence in any of the samples examined of the presence of anti-monkey-kidney precipitins.

In reviewing these promising results, the authors appreciate that none of the figures obtained can be fully accepted as a response to primary immunization, but they report that further trials are being undertaken in infants and children showing no evidence of antibodies, in order to determine the effectiveness of the irradiated vaccine as a primary immunizing agent. *H. J. Bensted*

317. **Improved Method for Cultivation of *Brucella* from the Blood**

W. BRAUN and J. KELSH. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 154–155, Jan., 1954. 5 refs.

A new technic for the recovery of *Brucella* cells from the blood of infected hosts is described. This technic employs filtration of laked blood specimens through membrane filters and permits the recovery of *Brucella* cells directly on solid media. The new method has proved to be at least as good as previously described blood culture methods and does not possess the disadvantage of cultivation in liquid media which is necessary in other methods. The membrane filter technic also appears to permit a quantitative estimation of the extent of bacteremia.—[Authors' summary.]

318. **Recovery of New Agent from Patients with Acute Respiratory Illness**

M. R. HILLEMAN and J. H. WERNER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 183–188, Jan., 1954. 14 refs.

The authors, working at the Army Medical Service Graduate School, Washington, D.C., report the recovery of a microbial agent, possibly a virus, from the throat washings of a patient with primary atypical pneumonia, during an epidemic among Service personnel in Missouri in the winter of 1952–3. The epidemic took the form of an acute respiratory-tract infection in which pulmonary changes were noted radiologically in some cases. The criteria for the diagnosis of primary atypical pneumonia are not given in this laboratory report, but serological tests were negative for influenza, Q fever, and psittacosis, and *Streptococcus* M.G. and cold agglutinins were absent.

The agent, designated RI-67, was found to have a cytopathogenic effect in roller-tube cultures of adult human tracheal epithelium, and in tube and bottle cultures of human epidermoid carcinoma cells. Infected cells showed degenerative changes in 24 hours and complete destruction in 48 hours. Serum-neutralizing and complement-fixing antibodies were found in the patient from whom the agent was isolated, and also in several other victims of the epidemic. Neutralization tests, using paired sera from other proven cases of viral pneumonia and primary atypical pneumonia, failed to show a rise in antibody titre against RI-67, but 50% of the serum samples showed a constant neutralizing-antibody level. Attempts to cultivate the agent in suckling mice, hamsters, young adult mice, guinea-pigs, and eggs (yolk, allantois, and amnion) were fruitless, and egg passage failed to produce cytopathogenic effects in tissue cultures.

[This agent is clearly unrelated to the organisms of influenza, Q fever, and psittacosis. What remains to be clarified is its precise relationship, if any, to the innumerable non-bacterial agents which are claimed to have been isolated from " primary atypical pneumonia " during the last 15 years.] *D. Geraint James*

Pharmacology

319. **The Role of Epinephrine and the Effect of Amine Oxidase Inhibitor (Marsilid) in Anaphylaxis in the Guinea Pig**

J. REBHUN and S. M. FEINBERG. *Journal of Allergy* [*J. Allergy*] **25**, 104–111, March, 1954. 34 refs.

In a study of the effect of adrenaline and iproniazid on anaphylactic shock, carried out at the Northwestern University Medical School, Chicago, guinea-pigs were sensitized to egg albumen either passively or actively, and shock produced by giving the antigen either as an aerosol or by injection. The animals were significantly protected against shock by 0·05 to 0·5 ml. of a 1-in-1,000 solution of adrenaline, whether this was given by single injection or by intravenous infusion lasting one hour. In a further group of guinea-pigs " marsilid " (iproniazid), which has been shown to be a complete inhibitor of amine oxidase *in vitro* and *in vivo* in rats and guinea-pigs, was injected in a dose of 50 mg. per kg. body weight 2 to 6 hours before induction of shock. It had no protective effect in anaphylactic shock, and it did not modify the protective action of adrenaline. *H. Herxheimer*

320. **A Critical Analysis of Cation-exchange Therapy**

A. G. SPENCER and H. G. L. LLOYD-THOMAS. *British Medical Journal* [*Brit. med. J.*] **1**, 597–603, March 13, 1954. 6 figs., 39 refs.

This paper from University College Hospital Medical School, London, reviews the use of cation-exchange resins in the treatment of 30 patients with cardiac oedema and 9 with renal oedema; most patients in both groups had failed to respond to other forms of treatment. All but 4 were treated with a sulphonated polystyrene cation-exchanger in combination with ammonium and potassium in the ratio of 3:1, the remaining 4 receiving a mixed cation–anion exchanger, 29% in the potassium phase. The first 4 patients treated received a hydrogen-cycle resin, but this caused buccal and gastric irritation and was given up when the other resins became available. A satisfactory response, as judged by significant loss of oedema and a loss of 7 lb. (3·18 kg.) or more in weight, was obtained in 21 (65%) of the 32 patients who had gross oedema initially. On the other hand side-effects, mainly gastrointestinal and rarely severe, occurred in 26 cases (67%), although major chemical disturbances were met with in only a few cases.

A very striking account is given of a case of Type-II nephritis in a woman of 44 who was given 60 g. of cation-exchange resin a day for 4 weeks. She lost 16 kg. in weight and 1,860 mEq. of sodium, her serum albumin level concurrently increasing from 1·8 to 4·8 g. per 100 ml. and the albuminuria declining from 16 parts to 1 part per 1,000. This therapeutic success followed a 3-week period during which no improvement had occurred with rest and a low-salt diet; a year later the patient was well, with normal renal function and normal urine. [No claim is, of course, made that the resin treatment was entirely responsible for this remarkable improvement, but the rapid clearing of a previously resistant oedema is in itself very striking.]

In the opinion of the authors, treatment with cation-exchange resins is indicated in congestive heart failure when standard treatment is not succeeding, when mercurial diuretics are not being effective or cannot be given because of toxicity, and also during convalescence to prevent recurrence of oedema. Resin treatment is also indicated in renal disease with massive oedema (Type-II nephritis or diabetic glomerulosclerosis) so long as the blood urea level is not raised. In such cases it should be given promptly, before prolonged immobilization has led to deterioration and thrombo-embolic episodes. Resin treatment should be combined with a low-salt diet and sufficient laxatives to ensure soft stools, but not watery diarrhoea. The need for biochemical control is stressed, especially as the treatment may lead to potassium depletion, even when the resin is partly in the potassium cycle; this can be corrected by the oral administration of potassium citrate. Resin treatment is contra-indicated in the presence of gastrointestinal disorders, renal failure, advanced liver disease, or pre-existing sodium or potassium depletion.

[This paper should be read in full by anyone using or planning to use ion-exchange resins in the treatment of oedema.] *D. A. K. Black*

321. **Cation Exchange in the Gastro-intestinal Tract**

A. G. SPENCER, E. J. ROSS, and H. G. L. LLOYD-THOMAS. *British Medical Journal* [*Brit. med. J.*] **1**, 603–606, March 13, 1954. 3 figs., 14 refs.

This paper from University College Hospital Medical School, London, describes observations which account for the disappointing failure of cation-exchange resins to remove sodium from the body in preference to other cations in spite of the fact that throughout a large part of the alimentary tract the resin is in contact with fluids containing a great preponderance of sodium over other cations. The greater affinity of these resins for divalent cations and for potassium is only partly responsible for this failure, for it was found that samples of resin obtained from the small bowel in 12 cases (3 of them post mortem) had in fact taken up large amounts of sodium. But samples taken from the proximal and distal colon in the cases examined at necropsy showed that in transit through the colon the greater part of this sodium is exchanged for potassium, calcium, and magnesium. The resin passed in the stools thus reflects the composition of fluid in the colon, which has been depleted of sodium by an active process of reabsorption.

These important findings were further confirmed by experiments on human subjects and on rats in which radioactive sodium and potassium were used to show

that the cations on the resin in each part of the gastro-intestinal tract are in dynamic equilibrium with those of the body. *D. A. K. Black*

322. **Cardiovascular and Respiratory Effects of Serpasil, a New Crystalline Alkalcid from *Rauwolfia serpentina* Benth., in the Dog**

J. H. TRAPOLD, A. J. PLUMMER, and F. F. YONKMAN. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **110**, 205–214, Feb., 1954. 3 figs., 16 refs.

"Serpasil" (reserpine), a colourless crystalline alkaloid extracted from the shrub *Rauwolfia serpentina*, is insoluble in water, but moderately soluble in a mixture of ethyl alcohol, propylene glycol, and water. In the study here reported the intravenous injection of 1 mg. of reserpine per kg. body weight in dogs anaesthetized with barbitone sodium caused a delayed and gradual fall in carotid arterial pressure, which was significantly different from changes seen in control animals 2 hours after an injection of the vehicle alone. The fall persisted for more than 5 hours, and was not affected by bilateral vagotomy and the injection of atropine or by giving a mixture of 95% oxygen and 5% carbon dioxide. Cardiac output, stroke volume, and cardiac index were still significantly reduced 3 to 4 hours later. Respiratory depression also occurred 30 to 90 minutes after the injection of reserpine, a decrease in respiratory rate and volume persisting for more than 4 hours. The depth of respiration generally remained constant or was increased.

Oxygen consumption was not increased by the drug. The difference between the oxygen content of arterial and venous blood was significantly increased 3 to 4 hours after the injection, this being the result of a decrease in venous oxygen content. The blood-pressure responses to doses of nicotine, acetylcholine, and carbamylcholine, and to increased intracranial pressure and peripheral vagal stimulation were not changed by reserpine. However, the response to doses of adrenaline was increased, and those to carotid occlusion and to central vagal stimulation were decreased. Doses of adrenaline in dogs anaesthetized with chloroform produced multifocal ectopic ventricular beats; after the injection of reserpine the arrhythmias produced by adrenaline were either converted to a nodal rhythm or were unchanged. In unanaesthetized dogs reserpine caused no significant fall in blood pressure. *P. A. Nasmyth*

323. **Investigation of the Toxicity of a Series of Dextran Sulphates of Varying Molecular Weight**

K. W. WALTON. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **9**, 1–14, March, 1954. 13 figs., bibliography.

Sulphuric esters of dextran with a molecular weight above 40,000 cause precipitation of plasma proteins *in vitro*, agglutination of platelets, and changes in the erythrocyte sedimentation rate. In the rabbit similar precipitation occurs after injection, because of the formation of non-specific complexes between the polysaccharide and the plasma proteins. These reactions are independent of the ordinary clotting process, which is delayed. The anticoagulant activity and toxicity of dextran sulphate of low molecular weight (7,500) are very similar to those of heparin.

From the University of Birmingham the author describes a careful investigation of the pathological processes underlying the toxicity of macromolecules. [The paper will give cause for thought among those who use toxicity tests for the standardization of drugs.] When a dextran sulphate with a molecular weight of 7,500 was given parenterally to rabbits there was no significant change in the plasma fibrinogen level, leucocyte count, or platelet count. Administration of dextran sulphate with a molecular weight of 47,000 or 458,000 resulted in a fall in plasma fibrinogen level and in the number of single platelets and leucocytes because of the formation of intravascular conglutination thrombi. The platelet and leucocyte counts later became normal, not by reversal of the agglutination process but by replacement of cellular elements from the bone marrow.

When animals died within a few minutes of intravenous injection of dextran sulphate having a high molecular weight, thrombi with a metachromatic framework characteristic of the dextran sulphate–fibrinogen complex were observed; they were mostly in the vessels of the lungs, but were also present in the kidneys, liver, and some other organs. Granules of metachromatic material were seen in large mononuclear and reticulo-endothelial cells. Death one to 4 hours after injection was due to acute haemorrhagic pulmonary oedema as a result of embolism; while death 12 hours to 7 days after injection was caused by haemorrhage secondary to infarction.

The histological findings thus indicated that the formation of a dextran sulphate–fibrinogen complex was responsible for the various toxic manifestations of different doses of the substance. A parallel was found between molecular size and the LD_{50} for mice.

The author concludes that a sulphated polysaccharide for use as a substitute for heparin should have an average molecular weight of about 7,500, and that there should be a limit to the size of the largest molecules present. *L. G. Goodwin*

324. **Influence of Inoculation Site Upon the Course of the "Anaphylactoid Reaction" to Dextran**

H. SELYE. *Journal of Allergy* [*J. Allergy*] **25**, 97–103, March, 1954. 1 fig., 13 refs.

At the Institute of Experimental Medicine and Surgery, Montreal, the author has produced an anaphylactoid reaction in a total of 280 rats divided into groups and given injections of a 6% dextran solution in different amounts and at different sites. This reaction is characterized by an acute serous inflammation similar to that seen in so-called egg-white oedema, and is limited to certain regions of the body, namely, the paws, snout, ears, and genitals, which the author terms "shock organs". The oedematous swelling of these organs could be easily elicited by the intravenous, intrapleural, or intraperitoneal injection of dextran in doses of 0·1 to 0·3 ml., while higher doses caused the response to decrease.

It was further shown that the injection of small amounts of dextran into one of the shock organs caused

swelling not only in that organ, but also in the more distant shock organs. If, however, comparable quantities were injected just outside a shock organ, or elsewhere subcutaneously, there was no local or distant response. The author discusses the possibility that some product of the reaction between dextran and the tissue of the shock organ is the cause of the anaphylactoid reaction of the distant shock organs. *H. Herxheimer*

325. **Quantitative Comparison of Dextromethorphan Hydrobromide and Codeine**

L. J. Cass, W. S. Frederik, and J. B. Andosca. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 291–296, March, 1954. 2 figs., 2 refs.

In a previous paper (*New Engl. J. Med.*, 1953, **249**, 132; *Abstracts of World Medicine*, 1954, **15**, 105) the authors reported that 4 mg. of dextromethorphan (D-3-methoxy-N-methylmorphinan) had approximately half the cough-suppressing effect of 17 mg. of codeine, but an accurate comparison of the two drugs was not possible under the conditions of the clinical trial then reported. A further trial was therefore carried out at Long Island Hospital, Boston, in which a comparison was made between the effects of 6-, 12-, and 18-mg. doses of dextromethorphan, 15 mg. of codeine, and a placebo, all of which were supplied as tablets of identical appearance and taste. Each medication was administered 3 times daily for 7 days, in random sequence, to 69 patients suffering from persistent cough. The degree of cough was assessed 3 times a day and given a numerical rating between 1 (occasional, barely troublesome) and 4 (incessant and distressing). From the total of all observations recorded, the average intensity of the cough during administration of each medication was calculated, the figures being 1·4887 for the placebo, 1·3655 for 6 mg. of dextromethorphan, 1·2833 for 12 mg. of dextromethorphan, 1·2629 for 15 mg. of codeine, and 1·2527 for 18 mg. of dextromethorphan. The differences in effectiveness between 12 and 18 mg. of dextromethorphan and 15 mg. of codeine are not statistically significant, and for practical purposes equal doses of dextromethorphan and codeine may be considered to be of equal antitussive activity. *Robert Hodgkinson*

326. **Evaluation of a New Cough Suppressant**

N. Ralph. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 297–303, March, 1954. 4 refs.

The antitussive activity of a synthetic drug, dextromethorphan (D-3-methoxy-N-methylmorphinan) was studied at Rush Hospital, Philadelphia, in a clinical trial on 144 patients, of whom 107 were suffering from pulmonary tuberculosis, 14 from acute bronchitis, 8 from chronic bronchitis, 8 from bronchiectasis, 4 from bronchial asthma, 2 from lung abscess, and 1 from bronchogenic carcinoma. All the patients suffered from cough, which was graded as barely troublesome in 14 cases, moderately troublesome in 65, marked in 47, and distressing and incessant in 18. The degree of relief provided by the drug in respect of frequency, intensity, and distress was assessed in each case 4 times a day by the nursing and medical staff separately as (1) no or slight relief, (2) moderate relief, or (3) marked to complete relief, the rating given being that of the majority in cases of difference.

Of 46 patients treated with 4 mg. of dextromethorphan 4 times daily, 13 (28·2%) obtained slight relief, 23 (50%) moderate relief, and 10 (21·7%) marked relief, while of 98 patients treated with 15 mg. 4 times daily, 10 obtained slight relief, 44 moderate relief, and 44 marked relief. The degree of relief was approximately the same in patients with cough of tuberculous and non-tuberculous origin.

In order to determine whether the drug had any untoward effect on the haematopoietic or urinary systems, 23 patients, including 11 without cough, were given dextromethorphan for a prolonged period, 22 receiving a total of 330 mg. in 31 days and one 198 mg. in 20 days. A further 20 patients received 75 mg. daily for 32 consecutive days. In both groups the blood pressure was measured, blood counts performed, and the urine examined initially, after 2 weeks' treatment, and at the end of the experiment. No untoward changes were noted and there was no evidence of the development of tolerance or addiction to the drug. Altogether, 183 patients received dextromethorphan, side-effects being reported by only 7 and consisting of nausea, vomiting, or dizziness. In one patient these symptoms necessitated discontinuation of treatment. *Robert Hodgkinson*

327. **Certain Cardiovascular Effects of Vasopressin (Pitressin)**

K. G. Wakim, C. Denton, and H. E. Essex. *American Heart Journal* [*Amer. Heart J.*] **47**, 77–83, Jan., 1954. 2 figs., 18 refs.

In consequence of reports of untoward effects following the use of vasopressin, the authors carried out an investigation at the Mayo Foundation, Rochester, Minnesota, in which doses of 0·1 to 1 unit of "pitressin" (vasopressin) per kg. body weight were given intravenously to 10 dogs either at once or by infusion over 30 minutes while the pulse rate, cardiac output, and the pulmonary venous and pulmonary and femoral arterial pressures were recorded. The injections caused an immediate slight increase in all pressures, with slowing of the pulse rate, but these changes were soon followed by a fall in arterial pressure and increased pressure in the left atrium and pulmonary artery, causing marked reduction in cardiac output. One dog died within 3 minutes of the injection.

The authors suggest that these results indicate production of an ischaemia of the myocardium, and that the administration of pitressin to any patient with a history of myocardial damage may be dangerous.

V. J. Woolley

328. **Immediate Blood Cell Response to Epinephrine**

L. H. Hamilton and S. M. Horvath. *American Journal of Physiology* [*Amer. J. Physiol.*] **176**, 311–318, Feb., 1954. 3 figs., 24 refs.

The haematological response of dogs to injection of adrenaline was studied at the State University, Iowa. Catheters were guided fluoroscopically into the abdominal

aorta, caudal vena cava, and right ventricle, so that samples of the blood entering and leaving the pulmonary system, the peripheral circulation, and the splanchnic bed were obtained. Blood was withdrawn through the three catheters immediately before, and during the first 2 minutes and the last 3 minutes of a 5-minute period after, a rapid intravenous injection of 500 μg. of adrenaline. Estimation of the erythrocyte and leucocyte counts, haematocrit value, and plasma protein concentration revealed no differences in samples obtained from the three sites. Briefly, the mobilization of erythrocytes and leucocytes was completed within two minutes. No relationship was found between the initial cell count and the magnitude of the increase in all cell types after injection of adrenaline, indicating that the cells were added to the circulation from reservoirs and not as a result of haemoconcentration. *G. B. West*

329. **Laboratory and Clinical Observations on Chlorpromazine (SKF-2601-A)—Hemodynamic and Toxicological Studies**

J. H. Moyer, B. Kent, R. Knight, G. Morris, R. Huggins, and C. A. Handley. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 283–290, March, 1954. 1 fig., 6 refs.

Preliminary clinical and laboratory studies having shown chlorpromazine (" thorazine ", " largactil ", " 4560 R.P. ", " SKF-2601-A ") to be an effective anti-emetic agent which acts by depressing the vomiting centre, its effects on cardiovascular and renal haemodynamics have been studied in experiments on animals carried out at Baylor University College of Medicine, Houston, Texas. The cardiac output, pulse rate, blood pressure, and peripheral vascular resistance were determined and the electrocardiogram (ECG) studied before and after the intravenous injection of increasing doses of chlorpromazine in anaesthetized dogs in the first series of experiments, and in a second series the effect of the drug on the glomerular filtration rate, renal plasma flow, and mean blood pressure was estimated, again in dogs.

It was concluded from these experiments that chlorpromazine is a hypotensive agent decreasing peripheral resistance and having a variable effect on cardiac output. No evidence of acute renal toxicity or alterations in renal haemodynamics was found, but the drug appeared to increase sodium and water excretion.

In addition, evidence of renal, hepatic, cardiac, or haematopoietic toxicity was sought in observations made on 38 healthy control subjects and on 25 patients under treatment for nausea and vomiting, chlorpromazine being given in various doses by both oral and intramuscular routes for one week or more. No evidence of hepatic or renal toxicity was found, while the only sign of possible haematopoietic toxicity was the appearance of granules in the leucocytes of one of the control subjects, the significance of which was doubtful. Changes in the ECG were observed in 2 cases, but these were in seriously ill patients and may have been due to the underlying disease. A greater response to the drug was noted in patients with hepatic disease, suggesting that the drug may normally be destroyed in the liver. There was no evidence of increased sodium excretion in the human subjects, who received doses of chlorpromazine which were relatively much smaller than those given in the animal experiments. *Robert Hodgkinson*

330. **Synthesis and Evaluation of a New Ganglionic Blocking Agent**

F. W. Schueler and H. H. Keasling. *Journal of the American Pharmaceutical Association* [*J. Amer. pharm. Ass.*] **43**, 98–101, Feb., 1954. 5 figs., 4 refs.

Earlier experiments (*J. Pharmacol.*, 1951, **103**, 222) had suggested that β-triethylammonium-(B′-triethylammonium ethyl) propionate dibromide (" racet ") exerted a greater effect on sympathetic than on parasympathetic ganglia. However, this seemed unlikely *a priori*, since both this compound and its methyl homologue include two muscarinic moieties in their structural formulae, suggesting some postganglionic parasympathetic stimulant action. This offered an alternative explanation for the differential action of racet as a depressant of sympathetic tone. A preliminary clinical trial in 20 patients with essential hypertension showed that the compound was not only useful as a ganglionic blocking agent, but did not give rise to constipation and mydriasis, which are side-effects of hexamethonium. The authors, at the State University of Iowa, therefore synthesized this compound and studied its value as a ganglionic blocking-agent.

The synthesis of racet from ethylene bromohydrin and β-bromopropionyl chloride is described in detail. The acute LD_{50} by intraperitoneal injection in mice exceeded 500 mg. per kg. body weight. In the dog, doses of 4 to 16 mg. per kg. body weight delayed the recovery of blood pressure after postural hypotension. It is claimed that racet, in its ability to antagonize the pressor effect of bilateral occlusion of the carotid artery or of injection of tetramethylammonium, has about the same potency as tetraethylammonium [no direct comparison is reported here]. In the cat, contractions of the nictitating membrane stimulated through the cervical sympathetic were blocked by 2 to 4 mg. of racet per kg. body weight. The authors suggest that the hypotensive action of the compound is unlikely to be due to cardiac depression, because in the isolated perfused rabbit heart 1 mg. caused some increase in amplitude, but no change in rate of beat or coronary flow. In a concentration of 1:10,000 it had a mild stimulant effect on isolated rabbit ileum, indicating its muscarinic action.

These findings suggest, in the authors' view, that racet is a ganglion blocking agent of the hexamethonium type " with a ' built-in ' muscarinic moiety ". Its muscarinic potency, however, is sufficient only to overcome the loss of parasympathetic tone produced by its action as a ganglionic blocking agent.

[It would be interesting to know whether the " selectivity " of action of racet on autonomic tone can be influenced by atropine. The abolition of the effect of acetylcholine on the isolated heart (as shown in one of the figures accompanying this paper) is also a point of some interest.] *Derek R. Wood*

Chemotherapy

331. **Research on the Mode of Action of Isoniazid.** (Ricerche sull'azione dell'idrazide dell'acido isonicotinico)

B. BESTA. *Annali dell'Istituto "Carlo Forlanini"* [*Ann. Ist. "Carlo Forlanini"*] **14**, 38–59, 1953. 18 refs.

In a study of the mode of action of isoniazid, carried out at the Forlanini Institute of Phthisiology, University of Rome, 20 healthy guinea-pigs were given doses of 10 to 15 mg. of isoniazid per kg. body weight per day for 2 to 3 months and then killed. Constant findings in the lungs were hyperaemia, capillary dilatation, interstitial oedema, and connective-tissue proliferation; in the kidney, tubular degeneration; and there was also lymphoid hyperplasia, especially in the spleen, and evidence of increased activity of the thyroid and pituitary glands and of the adrenal cortex.

Another large group of guinea-pigs were infected with human tubercle bacilli of medium virulence, treated with 10 mg. of isoniazid per kg. body weight daily, and killed in groups of 10 at 15-day intervals. The drug was shown to be rapidly and lastingly effective. Even when bacilli of highly resistant strains were used the evolution of the disease was slow, and lesions were restricted to the regional lymph nodes for periods up to 2 months. Hyperaemia of the upper part of the small intestine, often seen at necropsy in human subjects, did not occur unless there was a delay of 3 months between infection and the start of isoniazid therapy.

In the treatment of patients with pulmonary tuberculosis, the therapeutic activity of isoniazid was enhanced by the administration of ACTH or deoxycortone acetate, and reduced by that of cortisone. In a statistical study of results of sputum examination it was found that the proportion of patients remaining sputum-positive was 35% (a figure identical with that for a series examined in 1939–40). Tissue culture of organs from patients dying during treatment with isoniazid yielded positive cultures from the lung in 90% of cases, from the spleen in 32%, kidney in 27%, and liver in 17%. In a series of cases similarly investigated in the pre-chemotherapeutic era the figures for the lung were the same, but those for the other organs were higher.

The author concludes that the modification of the action of isoniazid by pituitary and adrenal hormones merits further study, and that the persistence of positive sputum findings in 35% of cases poses an important social problem. *D. Weitzman*

332. **Elaiomycin, a New Tuberculostatic Antibiotic. Biological Studies**

J. EHRLICH, L. E. ANDERSON, G. L. COFFEY, W. H. FELDMAN, M. W. FISHER, A. B. HILLEGAS, A. G. KARLSON, M. P. KNUDSEN, J. K. WESTON, A. S. YOUMANS, and G. P. YOUMANS. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 338–342, March, 1954. 3 refs.

333. **An Evaluation of Chemotherapeutic Agents in the Control of Experimental Infections Due to *Mycobacterium leprae murium***

G. L. HOBBY, J. H. HANKS, M. A. DONIKIAN, and T. BACKERMAN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 173–191, Feb., 1954. 9 figs., 11 refs.

The ultimate evaluation of antimicrobial agents used in the treatment of leprosy can be reached only after prolonged clinical trial, but as this is costly and time-consuming, the authors have developed a technique for rapid evaluation of the effect of such drugs on murine leprosy. In this paper from Harvard Medical School, Boston, they describe their method and discuss its usefulness for evaluating the likely effect of these substances in man. The method involves population counts of stainable acid-fast bacilli observed microscopically in a standard weight of spleen tissue prepared as a 10 or 20% suspension in water. Mice of the Dba strain were infected intraperitoneally with 0·4 ml. of a 2% tissue homogenate of *Mycobacterium lepraemurium* from the testes of rats which had been infected 6 months earlier. The population counts were made according to a standardized procedure [see original for details]. Organisms were detected in spleen suspensions 7 days after inoculation, and the counts rose steadily in the first 30 days, increasing sharply thereafter. In mice injected with heat-treated bacilli (100° C. for 5 minutes) the counts remained persistently low during the whole 60-day period of observation, although the spleens of these animals were never free from stainable, but presumably non-viable, bacilli. Evaluation of drug therapy seemed possible between 30 and 60 days after infection, the difference in count between animals given viable and those given heat-treated bacilli being great during this period. The reproducibility of the results was satisfactory within the same laboratory, but varied widely between two laboratories not using an identical technique. However, the relative effectiveness of two of the drugs tested was the same in both laboratories.

As judged by the technique described, the daily treatment of infected mice by oral or subcutaneous administration of oxytetracycline ("terramycin"), actithiazic acid, "promanide", amithiozone, 4:4′-diaminodiphenyl sulphone, and carbomycin was ineffective. Quantitative differences in activity of these several drugs were most apparent after treatment for at least 42 days following infection: at 30 days it was possible only to differentiate active from inactive compounds. Isoniazid and streptomycylidene *iso*nicotinyl hydrazine were the most effective drugs, followed by iproniazid, streptomycin, and viomycin in order of activity. Viomycin, as well as streptomycin, was active in combination with isoniazid, but no evidence of an additive or synergic action was obtained. Isoniazid was effective even when treatment was delayed for 8 to 21 days after infection,

a dose of 1 to 2 mg. per day being very active, although even 2·5 mg. twice weekly had an appreciable action. The effect of isoniazid persisted for 3 weeks after its administration was stopped.

The urgent need for a satisfactory method for the rapid and reliable screening of potential chemotherapeutic agents for treating human leprosy is stressed. The possibility of applying to man the results here described in mice is still uncertain, and the particular difficulties involved are discussed. The authors suggest that a satisfactory drug for the treatment of leprosy should: (1) be capable of inhibiting growth of mycobacteria; (2) be effective in the presence of body fluids and tissue; (3) be active against large masses of slowly multiplying micro-organisms; (4) be readily distributed throughout the body and capable of passing through all membranes without losing its effectiveness; and (5) be sufficiently non-toxic to allow of long-term treatment. They conclude that unless the murine strain of leprosy mycobacterium differs significantly from the human strain, a drug fulfilling the five criteria mentioned and effective against murine leprosy (as judged by the present technique) would be likely to be valuable in the treatment of human leprosy. The results suggest that isoniazid alone, or isoniazid with streptomycin or viomycin, should be effective in treating the human disease.

Derek R. Wood

ANTIBIOTICS

334. **Antiviral Action of a Mold Filtrate on Experimental Poliomyelitis in Cynomolgus Monkeys**
K. W. COCHRAN, G. C. BROWN, and T. FRANCIS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 104–106, Jan., 1954. 5 refs.

The crude filtrate of a penicillium mold, M-8450, was shown to have antiviral action in cynomolgus monkeys inoculated subcutaneously with the Mahoney strain of Type I poliomyelitis. Treatment with at least 100 ml. of this crude filtrate reduced the morbidity and increased the incubation period of infected animals. Less intensive treatment appeared to be less effective. The antiviral action of this substance appears to merit further study.—[Authors' summary.]

335. **Studies on the Haemato-encephalic Barrier. I. The Effects of Hyaluronidase with Special Reference to the Passage of Antibiotics.** [In English]
B. KELENTEI and I. FÖLDES. *Acta physiologica Academiae Scientiarum Hungaricae* [*Acta physiol. Acad. Sci. hung.*] **5**, 139–148, 1954. 5 figs., bibliography.

At the Medical University, Debrecen, Hungary, experiments were performed on 38 rabbits and 8 cats in which hyaluronidase was given either intravenously or intramuscularly 15 minutes before the administration of penicillin or streptomycin by the same routes, and its effect on the concentration of antibiotic in the cerebrospinal fluid (C.S.F.) obtained from the cisterna magna was studied. The concentration of antibiotic was determined bacteriologically either on agar plates or by dilutional methods, using *Staphylococcus aureus* for penicillin and *Bacterium coli* for streptomycin. After the administration of penicillin (2,000 to 15,000 units per kg. body weight) or streptomycin (0·02 to 0·05 g. per kg.) alone, effective concentrations could not be demonstrated in the C.S.F., but when the same doses were given together with hyaluronidase, measurable levels of both antibiotics were detected. With penicillin (5,000 units per kg.) the concentrations in the blood and C.S.F. after 15 to 30 minutes were about 4·0 and 1·0 μg. per ml. respectively, and with streptomycin (0·02 g. per kg.) the concentrations after 30 minutes were about 20 and 15 μg. per ml. respectively; neither antibiotic was detectable in the C.S.F. after 120 minutes.

The effect is regarded as being due to a specific action of the enzyme, since no penetration to the C.S.F. was observed when inactivated enzyme was used. The combined intravenous administration of histamine (0·2 mg. per kg.) and of hyaluronidase caused a greater increase in the permeability of the blood–brain barrier to the two antibiotics, but there was also a marked increase in the total nitrogen content of the C.S.F., indicating that the increased permeability was pathological. The antihistaminic drugs tripellenamine and antazoline in doses of 1 to 5 mg. per kg. did not exert any inhibitory effect on the action of hyaluronidase on the blood–brain barrier. No significant histological changes were demonstrable after the administration of hyaluronidase in sections of the lateral choroid plexus stained either with haematoxylin and eosin or with scarlet red.

R. Wien

336. **Studies on the Haemato-encephalic Barrier. II. The Effects of Histamine with Special Reference to the Passage of Antibiotics.** [In English]
I. FÖLDES and B. KELENTEI. *Acta physiologica Academiae Scientiarum Hungaricae* [*Acta physiol. Acad. Sci. hung.*] **5**, 149–161, 1954. 5 figs., bibliography.

The effect of histamine on the permeability of the blood–brain barrier to antibiotics was studied by methods similar to those described in the previous paper [see Abstract 335] in experiments on rabbits, cats, and guinea-pigs. As before, after the intravenous or intramuscular injection of penicillin and streptomycin alone, detectable concentrations of the antibiotics could not be found in the cerebrospinal fluid (C.S.F.). But the previous intravenous injection of histamine (0·2 mg. per kg.) caused the appearance of inhibitory concentrations of the antibiotics in the C.S.F., the highest level being attained 30 minutes after their injection; after 3 hours no antibiotic could be detected in the C.S.F. Moreover, when the histamine was withheld until the penicillin level in the blood reached its peak, an inhibitory concentration was obtained in the C.S.F. within 15 minutes, after which the penicillin levels in the blood and C.S.F. followed an approximately parallel course, the concentrations in the C.S.F. being about one-half those in the blood.

After 2,000 units of penicillin per kg. had been administered intracisternally none could be detected in the

blood, although an appreciable concentration was maintained in the C.S.F. for 8 to 10 hours, indicating the existence of a barrier in the reverse direction. However, when penicillin was given intracisternally in combination with histamine, the former was soon detected in the blood. The effect of histamine was specific and reversible, being antagonized by tripellenamine. After intravenous injection histamine could be found in the C.S.F., and histological examination of the lateral choroid plexus showed marked vacuolization of the epithelium; this was probably due to increased secretory activity and not to the presence of fat, since there was no staining with scarlet red. *R. Wien*

337. **Blood Dyscrasias Associated with Chloramphenicol. An Investigation into the Cases in the British Isles**
R. HODGKINSON. *Lancet* [*Lancet*] **1**, 285–287, Feb. 6, 1954. 1 fig., 4 refs.

An investigation into 31 cases of blood dyscrasia associated with the administration of chloramphenicol reported to the Antibiotics Committee of the Medical Research Council was undertaken by the manufacturers of the drug. There were 28 cases of aplastic anaemia and 3 cases of granulocytopenia, with 24 deaths. Necropsy usually revealed widespread haemorrhages and an aplastic bone marrow.

The majority of the patients affected had received more than 26 g. of chloramphenicol, which the author recommends as the maximum dose, to be spread over not more than 10 days, for adults. He recommends that children should not receive more than 100 mg. per kg. body weight daily for 7 days.

An accompanying chart indicates the number and duration of courses of chloramphenicol given in each of the 31 cases and their relation in time to the first symptoms of blood dyscrasia. [From this chart, it would seem that short repeated courses of chloramphenicol are dangerous as well as high dosage. Since there are other antibiotics with the same range of activity but without this serious toxic effect upon the bone marrow, it might be as well to use chloramphenicol only when other antibiotics have been found ineffective, and even then cautiously.] *D. Geraint James*

338. **Intramuscular Terramycin: Laboratory and Clinical Studies in Children**
C. O'REGAN and S. SCHWARZER. *Journal of Pediatrics* [*J. Pediat.*] **44**, 172–180, Feb., 1954. 1 fig., 9 refs.

The efficacy of intramuscular administration of " terramycin " (oxytetracycline) was studied in 50 children at St. Clare's Hospital, New York. Bioassays by the turbidimetric method showed that a therapeutic concentration of the antibiotic in the serum (0·3 μg. per ml., or more) was maintained for 12 hours after the intramuscular administration of 3 mg. per kg. body weight, and for 24 hours after a dose of 6 mg. per kg. (corresponding to a single oral dose of 22 to 33 mg. per kg.). A high therapeutic serum level was obtained almost as rapidly as after intravenous injection; diffusion into the cerebrospinal fluid, however, was poor. The results of intramuscular therapy in 45 patients with a great variety of infections were encouraging. The cases treated included pulmonary infections with *Staphylococcus aureus*, pneumococci, *Haemophilus influenzae*, *Bacterium coli*, and *Aerobacter aerogenes*, pharyngitis, tonsillitis, and otitis media due to *Staph. aureus*, *H. influenzae*, and *Proteus* spp., skin infections with *Staph. aureus*, and genito-urinary infections with pneumococci, *Neisseria gonorrhoeae*, *Proteus*, and staphylococci. A 16-day-old infant moribund with septicaemia due to *Bact. coli* recovered rapidly on treatment with oxytetracycline. In only 3 cases was there no response—namely, one case each of *H. influenzae* tonsillitis, staphylococcal bronchopneumonia, and patent ductus arteriosus with staphylococcal endarteritis.

The dose of oxytetracycline given ranged from 6 to 60 mg. per kg. daily, but in 70% of cases it did not exceed 12·5 mg. per kg. The authors recommend an intramuscular dose of 6 to 12 mg. per kg. every 24 hours for mild or moderately severe infections with pneumococci, streptococci, staphylococci, *H. influenzae*, and gonococci, and of 25 mg. per kg. for urinary infections with *Bact. coli* and *Proteus*. The drug was tolerated well by these children, whose ages ranged from less than one year to 13 years, the injection causing only slight local irritation which could be avoided by giving it deep into the buttock on alternate sides. *W. Mestitz*

339. **Antibacterial Action of Tetracycline: Comparisons with Oxytetracycline and Chlortetracycline**
B. D. LOVE, S. S. WRIGHT, E. M. PURCELL, T. W. MOU, and M. FINLAND. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 25–29, Jan., 1954. 3 figs., 6 refs.

The antibacterial action of tetracycline (" achromycin "), oxytetracycline (" terramycin "), and chlortetracycline (aureomycin) was tested *in vitro* at Harvard Medical School, Boston, against 257 strains of common pathogens. In general, the antibacterial action of these three analogues was very similar under the conditions employed. There were, however, significant quantitative differences in their action on certain individual strains. For example, oxytetracycline appeared to be most active against a large proportion of the strains of *Pseudomonas*, and tetracycline appeared most active against the few strains of *Proteus vulgaris* that were tested. Chlortetracycline was most active against a large proportion of strains of enterococci and *Staphylococcus aureus*.
A. W. H. Foxell

340. **Cross-resistance among 3 Tetracyclines**
S. S. WRIGHT and M. FINLAND. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 40–42, Jan., 1954. 10 refs.

Having shown [see Abstract 339] that the antibacterial action of the three tetracyclines was very similar, the authors investigated the development of cross-resistance against these three agents *in vitro*. Eight strains of organisms were subcultured 20 times in broth containing graded concentrations of either oxytetracycline or tetracycline. Each organism increased in resistance from 16- to 256-fold against the antibiotic

to which it had been exposed, to the other analogue, and also to chlortetracycline. (Chlortetracycline was not used for subculture because its rate of deterioration during the 3- or 4-day intervals at which the subcultures were made was too great.)

No cross-resistance or increase in sensitivity was observed to other agents such as penicillin, streptomycin, bacitracin, polymyxin, neomycin, or erythromycin as a result of the increase in resistance to the tetracyclines. Three strains of coliform bacilli, however, each showed significant cross-resistance to chloramphenicol following subcultures in either tetracycline or oxytetracycline, but similar cross-resistance was not observed in five Gram-positive coccal strains. *A. W. H. Foxell*

341. **Antibiotic Combinations and Resistance: Response of *E. coli* to Antibiotics, Singly and in Pairs**
S. S. WRIGHT, E. M. PURCELL, C. WILCOX, M. K. BRODERICK, and M. FINLAND. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 128–133, Jan., 1954. 2 figs., 4 refs.

At Harvard Medical School, Boston, 6 strains of *Bacterium coli* were repeatedly subcultured with the following antibiotics: streptomycin, chloramphenicol, " terramycin " (oxytetracycline), and polymyxin, either singly or in the 6 combinations of them in pairs. Resistance generally developed more slowly and to a lesser degree than when the same organisms were exposed to the same antibiotics individually. There were, however, wide variations depending mainly on the antibiotics used, and perhaps also on the strain of organism. It was also shown that resistance to neomycin appeared in organisms exposed to streptomycin, and to oxy- and chlortetracycline in those exposed to chloramphenicol. *A. W. H. Foxell*

342. **Observations on a Selected Antibiotic Combination**
H. F. FLIPPIN and G. M. EISENBERG. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 117–127, Feb., 1954. 16 refs.

The authors, writing from the Philadelphia General Hospital, discuss the reasons for using combinations of antibiotics and review the difficulties of their evaluation. They have been engaged for the past 3 years in an investigation of the inhibitory activity of antibiotics and antibiotic combinations against certain arbitrarily selected Gram-positive and Gram-negative organisms *in vitro*, the more effective combinations found being tested intensively against larger numbers of generically dissimilar bacteria *in vitro* and *in vivo*. Preliminary tests with penicillin, streptomycin, aureomycin (chlortetracycline), oxytetracycline, and chloramphenicol, separately and in 26 different combinations, against *Staphylococcus aureus* and *Klebsiella pneumoniae* Type A showed that aureomycin, oxytetracycline, and penicillin possessed both bacteriostatic and bactericidal synergism against the former, and aureomycin, oxytetracycline, and chloramphenicol a similar synergism against the latter. Further evaluation against some 260 different bacterial strains indicated that the combination of aureomycin, oxytetracycline, and chloramphenicol (in equal parts by weight) was the more effective. The comparative susceptibility of 2,173 individual strains of bacteria isolated from routine clinical specimens to this combination (COC) and to its separate constituents was then studied. *Streptococcus viridans* (107 strains), *Str. pyogenes* (38 strains), and *Diplococcus pneumoniae* (105 strains) were all uniformly susceptible to the individual antibiotics and the combination. About 30% of 843 strains of *Staph. aureus* and enterococci were susceptible to penicillin, 55 to 87% to the tetracyclines, and over 90% to the combination. Of a total of 1,093 Gram-positive strains, 95% (including penicillin-resistant strains) were susceptible to the combination. The susceptibility of Gram-negative organisms varied more widely; thus 47 strains of *Haemophilus influenzae* were all susceptible to the combination compared with 11·4% of 114 strains of *Pseudomonas aeruginosa* and 33% of 224 strains of *Proteus*. However, some 70% of a total of 1,080 Gram-negative strains were susceptible to the combination. Of the 2,173 strains of both types tested, 83% were susceptible to the combination, 75% to chloramphenicol, 56% to aureomycin, and 61% to oxytetracycline.

Comparison of the COC combination with erythromycin and carbomycin (" magnamycin ") showed all three to be equally active against *Staph. albus* and β-haemolytic enterococci, although erythromycin was slightly more active against *Staph. aureus* and α-haemolytic enterococci. Of about 600 strains of staphylococci and enterococci tested, over 90% were susceptible to all three agents, the incidence of susceptibility to erythromycin being slightly but significantly higher than that to carbomycin and to the combination. Clinical observations were made on cases of bacterial pneumonia, refractory infection of the urinary tract, and a miscellaneous group of diseases (including single cases of typhoid fever and of empyema due to *Bacteroides*). In cases of pneumococcal pneumonia the results of treatment with procaine penicillin (300,000 units intramuscularly 12-hourly) and with the COC combination (0·5 g. 6-hourly by mouth) were equivalent, but in *Klebsiella* pneumonia the COC combination was superior to penicillin. Of 12 selected patients with refractory infections of the urinary tract treated with 2 to 3 g. of the combination daily for 5 to 10 days, the infection resolved completely in 5, in 4 the pathogen was temporarily removed, and in 3 the results were equivocal; the authors suggest that the COC combination is worthy of further trial in such cases. *Malcolm Woodbine*

343. **Streptomycin Reactions. Relation to Exercise**
H. R. C. RICHES. *Lancet* [*Lancet*] **1**, 540–541, March 13, 1954. 1 fig., 4 refs.

Of 91 patients treated with intramuscular streptomycin 31 (34%) complained of toxic symptoms within a few hours of the injection. These reactions occurred less commonly when patients were resting. The blood-streptomycin level during exercise is generally higher than that found during rest. A period of rest following the administration of streptomycin may be of benefit to those patients who experience reactions.—[Author's summary.]

Infectious Diseases

344. **Results of a New Method of Treatment with Small-molecule Polyvinylpyrrolidone in Severe Tetanus.** (Ergebnisse einer neuartigen Therapie des schweren Tetanus mit niedermolekularem Polyvinylpyrrolidon)
R. SCHUBERT. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **79**, 179–180, Jan. 29, 1954. 1 fig.

Experiments were carried out at the University Medical Clinic, Tübingen, on guinea-pigs and mice from which the author concludes that the simultaneous injection of polyvinylpyrrolidone with antitoxin in cases of tetanus increases the activity of the latter in counteracting the effects of the toxin. Clinical observations by the author and others are quoted, in which cases which did not respond to the usual treatment with large doses of antitoxin showed definite improvement after the intravenous injection of 6% " periston N ". It is suggested that the effect of the polyvinylpyrrolidone is not only on the tetanus toxin in the blood stream, but also on the toxin which has already reached the nerve cells and is out of the reach of antitoxin. *Franz Heimann*

345. **Erythromycin Therapy of Respiratory Infections. I. Controlled Studies on the Comparative Efficacy of Erythromycin and Penicillin in Scarlet Fever**
T. H. HAIGHT. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43**, 15–30, Jan., 1954. 6 figs., 26 refs.

The efficacy of erythromycin and of penicillin in the treatment of scarlet fever was studied in 208 patients admitted to the U.S. Naval Training Center, Bainbridge, Maryland, during January and February, 1953. A presumptive diagnosis of scarlet fever had been made in all cases, but none of the patients had received antibiotic therapy during the 2 weeks preceding the investigation. Erythromycin was given by mouth to 78 patients in a dosage of 200 mg. on admission and then 4-hourly for 10 days. Aqueous crystalline benzylpenicillin was administered by intramuscular injection to 78 patients in a dosage of 300,000 units on admission and then 12-hourly for 10 days. A placebo identical in size and colour with the erythromycin tablets was given to 52 patients for the first 10 days, and then, in order to reduce the streptococcal carrier rate, they received penicillin as above until the time of discharge from hospital.

The three groups were comparable as regards history of tonsillectomy, symptoms, and incidence of allergy and recent respiratory infection. The chief complaint was of sore throat (although only 14% of the patients showed exudate in the nasopharynx). Two-thirds of the patients complained of headache. The classic " strawberry tongue " was present in only 16%. Throat culture was positive for Group-A haemolytic streptococci in over 90% of the patients in each of the three groups, all but 3 of the 201 strains isolated being Type 19. The rise in antistreptolysin-O titre was much less in the two groups given antibiotic therapy than in the group receiving a placebo. The effect of treatment on the duration of the rash and fever, on the leucocytosis, and on eradication of the streptococcus from the nose and throat is described in detail. Clinical recovery was less rapid in the patients receiving a placebo than in those given antibiotic therapy; however, when the total duration of the illness was considered, the difference between the treated and untreated groups was less marked. Of the patients receiving erythromycin 3 developed mild gastrointestinal symptoms, and of those receiving penicillin 12 developed a rash which was indistinguishable from that of scarlet fever; a similar rash or an urticarial reaction was noted in 8 of the patients receiving the placebo.

The author suggests that this trial provides convincing evidence of the efficacy of erythromycin against the haemolytic streptococcus. *T. Anderson*

346. **Recovery of Muscular Strength after Poliomyelitis**
W. RITCHIE RUSSELL and M. FISCHER-WILLIAMS. *Lancet* [*Lancet*] **1**, 330–333, Feb. 13, 1954. 8 figs., 6 refs.

In the acute stage of poliomyelitis the affected anterior horn cells can be identified almost as soon as paralysis develops; those destroyed by the virus disappear completely in a few days, others become normal in appearance in 4 or 5 weeks. No histological change has been observed to account for the recovery of muscle function, which may take at least one year. In the active stage of the disease 90% of muscles which subsequently recover respond to faradic stimulation of the nerve, whereas 78% of permanently paralysed muscles cease to react to nerve stimulation within 10 days of the onset of the illness.

At Stoke Mandeville Hospital, Buckinghamshire, the authors have studied muscle recovery in 70 selected patients with paretic but not completely paralysed muscles. Treatment in the acute phase was with complete physical rest, the posture being altered every 2 hours and the joints moved passively every 4 hours. Hot packs were applied in some cases to relieve muscle pain. Active movements and sling exercises were started after 3 weeks. At 6 to 8 weeks from the onset standing and walking between parallel bars was begun, with appropriate body support if necessary, special attention being paid to faulty habits and posture. In some cases, in addition to the normal routine, a special programme of intensive exercises was carried out, which consisted in exercising one muscle group for five minutes once an hour for 10 hours a day, this procedure being continued for one week.

The muscles studied were the extensors and flexors of the elbow and knee, the respiratory muscles, and the muscles of grip. Muscle strength was recorded by the resistance of a simple spring balance; the strength and fatigue of the muscles of grip were recorded on a dynamo-

meter; and progress of the respiratory muscles was assessed by measurement of vital capacity.

There was a steady improvement in the strength of all the muscles studied; the rate and amount of recovery varied and was not related to treatment. Improvement began 3 to 4 weeks after the onset of the illness and continued for 30 or 40 weeks, when it slowed or, in some cases, ceased. Neither serious weakening of the exercised muscles nor alteration in the rate of recovery was observed during the period of intensive exercise; in some cases there was an increase in the rate of recovery after the exercise period.

It is suggested that in poliomyelitis active exercises should be encouraged after the first 4 weeks, but that further study is necessary to determine the intensity of the exercises to be employed. *J. B. Millard*

347. **The Bristol Respirator**
J. MACRAE, A. M. G. CAMPBELL, R. PONTING, and J. E. BENDY. *Lancet* [*Lancet*] **1**, 704–707, April 3, 1954. 5 figs., 2 refs.

348. **A New Cabinet Respirator**
J. F. GALPINE. *Lancet* [*Lancet*] **1**, 707–709, April 3, 1954. 3 figs., 2 refs.

349. **ACTH Therapy in Acute Viral Hepatitis**
V. M. SBOROV, B. GIGES, I. C. PLOUGH, and W. MANDEL. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43**, 48–57, Jan., 1954. 7 figs., 11 refs.

An attempt was made at the Walter Reed Army Medical Center, Washington, D.C., to assess the therapeutic value of ACTH (corticotrophin) in viral hepatitis. The patients studied, mostly young soldiers, were seen over a period of 4 years, and many had hepatitis of long incubation period following blood or plasma infusion. They were not a homogeneous group, but included only cases with less than 7 days' jaundice. After the first 12 had been given ACTH treatment alternate patients were used as controls, a total of 49 treated and 36 control subjects being studied. Five different treatment schedules were employed, the authors altering their method as they acquired experience. The first 19 patients were given ACTH either subcutaneously or intravenously for 10 days. But as improvement ceased when the ACTH was stopped, all the remainder were given ACTH intramuscularly or intravenously (mostly intravenously) until their serum bilirubin level returned to normal. Intravenously, a solution of 20 mg. of ACTH in 500 ml. of 5% glucose was used, given as a slow drip infusion. In the last and most successful schedule used, the dose was 10 to 20 mg. daily at first, and was gradually reduced to 2·5 to 5 mg. by the end of the period of treatment. Of the control subjects, 15 had no special treatment and 21 received 5% glucose solution intravenously until their serum bilirubin level had returned to normal.

Progress was assessed by determination of the serum bilirubin level and urinary bilirubin content, and by periodical performance of the thymol turbidity and cephalin flocculation tests and liver biopsy. A fall in serum bilirubin level occurred within 48 hours of starting intravenous ACTH therapy in all cases, but the improvement could be maintained only by continuous treatment. The results of the liver function tests returned to normal more rapidly (with wide variations) in the majority of the treated cases than in the controls, but the authors suggest that this may have been due to a non-specific suppression of the serum reactions and therefore not a true guide to the patient's progress. On comparison of the biopsy findings in treated and control subjects " the differences noted were not sufficiently clear-cut to be quantitated even on a rough scale ".

[It is difficult to draw a definite conclusion from these investigations. In the variously treated groups and the two control groups the disease differed materially in severity, as judged by the maximum serum bilirubin levels. Whenever comparison is possible, however, the advantage is clearly in favour of the groups given prolonged treatment with intravenous ACTH, although the numbers are too small to be significant. A trial on a larger scale is indicated, with better grouping according to severity.]
L. J. M. Laurent

350. **Steroid Excretion Patterns in Acute Viral Hepatitis, with and without Adrenocorticotrophin Infusion**
R. E. PETERSON, S. GUERRA, and V. M. SBOROV. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43**, 58–69, Jan., 1954. 9 figs., 32 refs.

It is generally accepted that the liver plays a major role in inactivating the adrenal cortical hormones by oxidation to 17-ketosteroids and that in liver disease the urinary 17-ketosteroid excretion is diminished. In order to determine how far this may be due to a decreased production of corticosteroids and how far to impaired conversion into 17-ketosteroids in the liver, a series of experiments were undertaken at the Walter Reed Army Medical Center, Washington, D.C. The authors first studied the urinary excretion of corticosteroids and 17-ketosteroids in various forms of liver disease, including 38 cases of acute viral hepatitis, and confirmed the findings of previous workers that the excretion of corticosteroids in such cases is the same as in normal individuals, whereas that of 17-ketosteroids is much diminished. They then studied the excretion of the same steroids by 16 patients with acute hepatitis given a daily intravenous injection of 10 to 20 mg. of ACTH (corticotrophin). They found that the excretion of corticosteroids was greatly increased, as in normal persons, but that 17-ketosteroid excretion followed 3 different patterns: (1) a normal increase in 4 cases; (2) a minimal increase or no change in 5 cases; and (3) a continued low level of excretion in the active phase of the disease followed by a slow rise during convalescence in 7 cases. They conclude that as the urinary corticosteroid excretion is normal in infective hepatitis and the normal increase takes place on giving ACTH, there is no evidence of hypoadrenalism, and that conversion of corticosteroids into 17-ketosteroids by the liver is defective.

[It is to be hoped that the response of 17-ketosteroid excretion to intravenous ACTH does not develop into another routine test for evidence of liver dysfunction.]
L. J. M. Laurent

Tuberculosis

351. **Skin Lesions and Deafness in Disseminated Tuberculosis**
A. W. LEES and I. B. MUNRO. *British Medical Journal* [*Brit. med. J.*] **1**, 496–499, Feb. 27, 1954. 8 refs.

The diagnostic significance of skin lesions in disseminated tuberculosis is emphasized by reference to 8 cases seen at Ruchill Hospital, Glasgow, in 3 of which increasing deafness was also a marked feature.

In 4 of the cases the cutaneous lesions varied from papules and pustules with reddened skin to lesions resembling acne vulgaris and indolent furuncles. The commonest sites were the front and back of the chest, behind the ears, and the forearms. Examination of biopsy specimens showed necrosis in one case and areas of caseation in the remaining 3 cases. The authors state that where necrosis is a prominent feature involvement of the bone marrow may give rise to abnormalities of the peripheral blood. In the remaining 4 cases there were subcutaneous nodules, which became fluctuant and from which acid-fast bacilli were cultured. There was no evidence of tuberculous meningitis or of middle-ear disease in the 3 patients who became deaf, and the authors attribute the deafness to toxaemia.

The variety of clinical features which may be present in disseminated tuberculosis is discussed. The authors consider that biopsy of any skin lesions present, of the sternal marrow, or of the liver may assist early diagnosis in these cases. *D. J. Pearce*

352. **The Relationship of Stress, Adrenocortical Function, and Tuberculosis**
E. R. CLARKE, D. W. ZAHN, and T. H. HOLMES. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 351–369, March, 1954. 7 figs., bibliography.

353. **Clinical and Histopathologic Study of the Effects of Antimicrobial Therapy in Tuberculosis**
L. J. WALLNER, J. R. THOMPSON, and M. R. LICHENSTEIN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 247–260, Feb., 1954. 7 figs., 6 refs.

At the Municipal Sanitarium, Chicago, serial biopsies of tuberculous lesions in the mouth, pharynx, and larynx were taken before, during, and after treatment with dihydrostreptomycin, streptomycin, isoniazid, PAS, thiacetazone, or various combinations of these drugs. The first change noted was the cessation of pain within 48 to 96 hours after starting treatment. Thereafter there was also objective evidence of improvement in the form of a gradual decrease of the oedematous swelling and infiltration; this was followed by epithelization of the ulcerated areas, with disappearance of the tubercle bacilli from the sputum after approximately 4 months' treatment. Improvement was most rapid in patients treated with dihydrostreptomycin, streptomycin, or isoniazid. With PAS improvement was slower, and thiacetazone was ineffective in the single case treated. Patients treated with cortisone or corticotrophin (ACTH) showed no objective evidence of improvement. *Franz Heimann*

354. **The Use of " Hinokitiol " (m-*iso*-Propyltropolon) in the Treatment of Tuberculous Fistula and Pulmonary Tuberculosis.** (Über therapeutische Anwendungen des Hinokitiols (m-Isopropyltropolon) bei tuberkulöser Fistel und Lungentuberkulose)
S. KATSURA. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **110**, 522–525, 1954. 3 figs., 11 refs.

An account is given of the use of " hinokitiol " (4-*iso*-propyl*cyclo*hepatrien-2:4:6-ol-2-on-1) in the treatment of an unspecified number of cases of advanced pulmonary tuberculosis and 12 cases of tuberculous anal fistula in adults at the Medical Clinic of the University of Niigata, Japan. The substance is slightly active against the tubercle bacillus, which is stated to develop no resistance to it. The clinical results were equivocal in pulmonary tuberculosis, though cavities are stated to diminish in size with local treatment. Of the cases of fistula, 6 are stated to have been healed and 6 much improved with hinokitiol treatment.

[The absence of controls and the paucity of details make it impossible to evaluate the claims made for this drug.] *J. Lorber*

355. **The Diagnostic Value of B.C.G. Tuberculin in Naturally Infected Children and Children Vaccinated with B.C.G.** (BCG-Tuberkulin. Sein diagnostischer Wert bei natürlich-infizierten und BCG-geimpften Kindern)
K. QUAISER. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **110**, 507–516, 1954. 11 refs.

The properties of B.C.G. tuberculin were compared with those of the standard old tuberculin in four groups of children at the University Children's Clinic in Graz, Austria. Tuberculin tests were simultaneously performed by von Pirquet's technique with standardized B.C.G. tuberculin and with old tuberculin. In a group of 117 children with active tuberculosis no difference was observed in the incidence of positive reactions (89·7%) to the two preparations. Among 112 children who were considered to have inactive tuberculosis the incidence of positive reactions fell, but positive reactions were more frequent with B.C.G. tuberculin (79·4%) than with old tuberculin (70·5%). Among 130 children who had been vaccinated with B.C.G. 1 to 2 years earlier even greater differences were found: B.C.G. tuberculin gave positive results in 87·6% and old tuberculin in only 63%. The last group consisted of 145 children who were known to have been infected with tuberculosis, but had subsequently become tuberculin negative and

had then been vaccinated with B.C.G. One to two years after vaccination 94·4% gave a positive reaction to B.C.G. tuberculin and 86·2% to old tuberculin. In all four groups the positive reaction to B.C.G. tuberculin was stronger than that to old tuberculin more often than the reverse. This difference was slight in patients with active tuberculosis, more definite in patients with inactive tuberculosis, and pronounced in the two B.C.G.-vaccinated groups (in the ratio of 6:1).

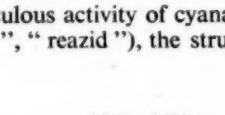
It is suggested that B.C.G. tuberculin may well replace old tuberculin as a diagnostic tool. By using the two tests together some indication may be gained whether a positive reaction is due to natural infection or B.C.G. vaccination, although absolute differentiation is not possible. The author could not detect any difference in the colour of the papule between naturally infected and vaccinated patients.

[This was a carefully controlled trial carried out on sufficiently large groups of patients. The conclusions in regard to differences between the reaction to B.C.G. tuberculin and to old tuberculin, however, probably apply only to the old tuberculin used by the author, which appears to have been of low potency as over 10% of the children with active tuberculosis gave a negative reaction to the 2nd-strength Pirquet test. Similar differences may not be demonstrable with other, more active, preparations of old tuberculin.] *J. Lorber*

RESPIRATORY TUBERCULOSIS

356. **Preliminary Report on "Reazid" in Experimental Tuberculosis.** (Erste Erfahrungen mit Reazide bei experimenteller Tuberkulose)
W. HARTL. *Schweizerische Zeitschrift für Tuberkulose* [*Schweiz. Z. Tuberk.*] **11**, 65–76, 1954. 1 fig., 4 refs.

The antituberculous activity of cyanacetic acid hydrazide ("cyanazid", "reazid"), the structural formula of which is



has been investigated *in vitro* and *in vivo*. *In vitro* cyanazid inhibited the growth of tubercle bacilli in concentrations varying according to the medium used for culture. Organisms resistant to streptomycin, PAS, or isoniazid were sensitive to cyanazid, but secondary resistance to cyanazid developed rapidly—after 4 passages in some cases. *Mycobacterium tuberculosis* H37Rv was usually inhibited by concentrations of 5 to 10 μg. per ml., but the bovine Vallée strain was much less sensitive.

Experiments were performed *in vivo* on five groups of guinea-pigs, each experiment lasting 106 days after which the surviving animals were killed and subjected to necropsy. The groups were treated as follows. (1) Not inoculated with tubercle bacilli, but given cyanazid in doses gradually increasing from 12 mg. to 50 mg. per kg. body weight (3 animals); these suffered no toxic effects. (2) Untreated infected controls (5 animals); all developed widespread tuberculosis. (3) Infected and treated immediately with cyanazid (12 to 24 mg. per kg. daily) (3 animals); none developed tuberculosis. (4) Treated with cyanazid (12 to 30 mg. per kg. daily) starting on the 30th day after infection (5 animals); one died with scattered tuberculous lesions, but the remainder were protected against all but local infection. (5) Treated with streptomycin (15 mg. per kg. daily) starting on the 30th day after infection (4 animals); 2 died, but with localized disease only, and in 2 there was no sign of disease. The degree of protection afforded by streptomycin appeared, on the whole, better than with cyanazid.

[Although the results appear promising, the number of animals in each group is unfortunately too small for any but guarded conclusions to be drawn.] *J. Lorber*

357. **Preliminary Report on the Treatment of Pulmonary Tuberculosis with Cyanacetic Acid Hydrazide ("Reazid").** (Vorläufige Mitteilung über Beobachtungen bei Behandlung der Lungentuberkulose mit dem Hydrazid der Cyanessigsäure (Reazide))
H. SCHEU. *Schweizerische Zeitschrift für Tuberkulose* [*Schweiz. Z. Tuberk.*] **11**, 77–91, 1954. 6 figs., 1 ref.

The author reports in detail 11 cases of pulmonary tuberculosis which were treated with "cyanazid" [see Abstract 356] in doses of 5 to 8 mg. per kg. body weight daily and in which treatment had been concluded. Most of the patients had already been treated with other chemotherapeutic agents. The patients' general condition gave a uniform impression of improvement which was similar in degree to that usually observed during isoniazid treatment, but objective evidence of improvement was less definite. However, in 3 cases the sputum, previously persistently positive, became negative for tubercle bacilli, and radiological improvement was noted in 6 cases. Several patients complained of side-effects, including paraesthesiae, nervousness, and nausea.

[No valid conclusions can be drawn from this paper, partly because the number of patients treated was small and the period of observation short, but chiefly because no attempt was made to include any form of control group or to make an objective assessment.] *J. Lorber*

358. **The Morbid Anatomy of Pulmonary Tuberculosis after Treatment with Isoniazid and after Combined Therapy.** (Aspetti anatomopatologici della tubercolosi polmonare trattata con isoniazide e con terapia combinata)
C. PANÀ. *Annali dell'Istituto "Carlo Forlanini"* [*Ann. Ist. "Carlo Forlanini"*] **14**, 15–37, 1953. 8 figs., 12 refs.

In this paper from the Forlanini Institute of Phthisiology, Rome, the author describes the necropsy findings in 100 cases of pulmonary tuberculosis which had been treated with isoniazid, either alone or in combination with antibiotics or other chemotherapeutic agents.

Intestinal congestion, especially of the upper part of the small bowel, was found in 90% of cases and was most marked in those still receiving chemotherapy at the time

of death. The congestion was patchy, with sharp margins to each area, but these areas bore no relation to any specific tuberculous lesions. When the latter lesions were present they differed in appearance from the classic transverse ulcer with undermined edges, showing instead small, shallow areas of ulceration up to 1 cm. in diameter. The author considers these to have been of recent origin, and probably due to tubercle bacilli with a high degree of resistance.

Dissemination of bacilli by the blood stream was found to be greatly reduced in comparison with that in a previous series studied in the pre-chemotherapeutic era (Daddi and Panà, *Ann. Ist. "Carlo Fornanini"*, 1938, **2**, 1). Spread occurred to the liver in 44% of cases as compared with 78% in the earlier series, to the kidney in 8% (previously 32%), and in no case did the spleen show typical lesions (as seen in the previous series), although cellular infiltrations were noted.

In the lungs, cavity surfaces were clean, their caseous linings having separated. Pericavitary and intracavitary haemorrhages were common (and terminal haemoptyses had frequently been noted clinically). In the lymph nodes (as generally in all organs) tuberculous lesions tended to lose their specific histological appearance and instead appeared as lymphocytic infiltrations.

D. Weitzman

359. **Pyrazinamide–Isoniazid in Tuberculosis**
W. McDERMOTT, L. ORMOND, C. MUSCHENHEIM, K. DEUSCHLE, R. M. McCUNE, and R. TOMPSETT. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 319–333, March, 1954. 9 refs.

The authors present, from the New York Hospital–Cornell Medical Center, New York, a preliminary report of their investigations of the effects of pyrazinamide and isoniazid, administered together, on infected mice, together with the results of a clinical study of the administration of these drugs to patients with pulmonary tuberculosis. [The use of pyrazinamide, a compound in the nicotinamide series, was first reported by Yeager *et al.* (*Amer. Rev. Tuberc.*, 1952, **65**, 523; *Abstracts of World Medicine*, 1952, **12**, 407).]

In the first part of their study the present authors, using a microbial enumeration technique, found that the administration of isoniazid to mice infected with tuberculosis caused a sharp fall in the population of tubercle bacilli in the lungs—sometimes below the limits of detection—whereas in the spleen, after an initial decrease, the population stabilized despite continued administration of the drug although, it is pointed out, the persisting organisms were not drug-resistant in the ordinary sense. In contrast, the combined administration of pyrazinamide and isoniazid caused the fall in the numbers of bacilli in the spleen to continue, as in the lung, until they could no longer be detected. The synergistic action of the two drugs appeared to sterilize the spleen in a manner quantitatively and qualitatively different from that of any other antituberculous agent.

The combined treatment was then applied to 81 adolescent and adult patients with advanced or moderately advanced, bacteriologically positive tuberculous lesions in the lung. Pyrazinamide was given in a daily dosage of 50 mg. per kg. body weight and isoniazid in a daily dosage of 5 mg. per kg., both drugs being given orally in equally divided doses twice daily. The patients were kept at rest in bed, and liver function tests performed regularly. The first 16 patients received the two drugs together for about 6 months, isoniazid alone being given thereafter. As evidence of hepatic toxicity occurred, however, the period of pyrazinamide administration was shortened to 90 days and later stopped altogether.

Of the 53 patients treated for 3 months or longer, there was sustained absence of tubercle bacilli from sputum and gastric washings in 47 (90%), and substantial radiological improvement in 39 (75%). Two patients not included in the above group died from tuberculosis soon after treatment began, and a third died of drug-induced hepatitis on the 55th day of treatment; 5 other cases of non-fatal hepatitis (2 severe) also occurred. The authors are unwilling to commit themselves as to the degree of responsibility of the two drugs, separately or in combination, for the hepatitis, but conclude that in the dosage used the regimen is inadvisable. Nevertheless, they are of the opinion [which appears justified] that, taking into account the animal experiments, the antimicrobial action of pyrazinamide with isoniazid is quantitatively superior and qualitatively unique among antituberculous chemotherapeutic agents.

[These results should be compared with those reported by Campagna *et al.* (see Abstract 360).]

R. J. Matthews

360. **Observations on the Combined Use of Pyrazinamide (Aldinamide) and Isoniazid in the Treatment of Pulmonary Tuberculosis. A Clinical Study**
M. CAMPAGNA, A. A. CALIX, and G. HAUSER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 334–350, March, 1954. 8 figs., 13 refs.

In this report, based on the results of 18 months' observation, the authors describe the treatment of 21 cases of active, far-advanced pulmonary tuberculosis at the Tuberculosis Clinic of the New Orleans Health Department with isoniazid combined with pyrazinamide ("aldinamide"). In all cases the sputum was positive for tubercle bacilli, and most of the patients had failed to respond to streptomycin, PAS, and various forms of collapse therapy. Initially, four doses of 350 mg. of pyrazinamide were given daily, but this dosage was later increased, a daily total of 3 g. being given; isoniazid was administered concurrently in a daily dose of 4 mg. per kg. body weight. Regular examinations of the blood and urine and tests of liver function were performed; the detailed results of these are tabulated and a number of radiographs are reproduced.

In all but 2 patients the sputum became negative within 4 months and has remained so (the investigation being started in June, 1952). Tubercle bacilli from the 2 patients with positive sputum showed resistance to isoniazid *in vitro*. There was radiological improvement in the majority of cases, especially in those with soft, exudative lesions of recent origin, but also in some cases with fibrotic lesions in which improvement was not expected. All showed an increase in the erythrocyte

count, which was accompanied by an increase in the haemoglobin concentration in many cases. A substantial improvement in weight (average 13 lb. (5·9 kg.)) occurred in all except the 2 persistently sputum-positive patients. The authors conclude that in 8 cases the disease can now be considered inactive, and that most of the others are no longer a danger to the community. The few toxic effects caused by the drugs, namely, joint pains (10 cases), headache (2), mild jaundice (3), and difficulty in micturition (3) were not of serious consequence.

[These results, especially the absence of serious toxicity, are in favourable contrast with those reported by McDermott *et al.* (see Abstract 359). This may have been due to the smaller doses given, or to variation in susceptibility of the patients—the above series of 21 cases included 13 negroes—but more information would be required for a critical comparison.]

R. J. Matthews

361. **Tuberculomata and Segmental Resection.** (Tuberculomes et résection segmentaire)
A. MARMET, M. JAUBERT DE BEAUJEU, J. PLANE, M. MICHEMBLE, and M. PETIT. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **18**, 65–73, 1954. 3 figs., 6 refs.

362 (*a*). **The Appearances and Causation of Bullous Cavities during the Treatment of Pulmonary Tuberculosis with Antibiotics.** (Variétés d'aspect et conditions d'apparition d'images bulleuses au cours du traitement de la tuberculose pulmonaire par les antibiotiques)
E. BERNARD and J. CARRAUD. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **17**, 1021–1036, 1953. 11 figs., 8 refs.

362 (*b*). **Bullous Cavities. Anatomical and Clinical Observations.** (Cavernes bulleuses. Documentation anatomo-clinique)
P. GALY, M. BÉRARD, P. ARRIBEHAUTE, R. G. TOURAINE, and —. DE SAINT-FLORENT. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **17**, 1037–1045, 1953. 4 figs.

362 (*c*). **Tuberculous Cavities of Bullous Form.** (Cavernes tuberculeuses à forme bulleuse)
P. PRUVOST, J. DELARUE, A. MEYER, and —. DEPIERRE. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **17**, 1046–1050, 1953. 3 figs.

362 (*d*). **Pulmonary Bullous Appearances.** (Images bulleuses pulmonaires)
—. SIMONIN, —. GIRARD, —. LOCHARD, and —. SADOUL. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **17**, 1051–1054, 1953. 4 figs.

362 (*e*). **So-called Bullous Cavities.** (Les cavernes, dites " bulleuses ")
A. BERNOU. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **17**, 1055–1057, 1953.

This series of papers draws attention to the appearance of bullous cavities in the lung during the chemotherapy of pulmonary tuberculosis. Bernard and Carraud report 4 cases of acute disease in young persons who were all treated with streptomycin (1 g. every 3 days), isoniazid (5 mg. per kg. body weight daily), and PAS (15 g. daily). After 3 to 4 months the sputum became negative for tubercle bacilli and radiologically the infiltration was less, but the radiograph showed one or more thin-walled bullous cysts which might be in relation to a pre-existing cavity or appear in other situations in the lung. These bullous cavities varied in size from time to time and might also fuse together. One patient underwent pulmonary resection, and a large, thin-walled cavity of rubbery consistency was found, its lining showing no areas of caseation except in two diverticula. The authors consider that in most cases the appearance of these cavities is a favourable sign and suggest that in the absence of any other indication for surgery they should be left untouched, although the ultimate prognosis in such cases is uncertain.

Galy *et al.* report 3 cases, together with the results of examination of the resected specimens. The cavities found were again thin-walled and of a rubbery consistency, the lining being of amorphous fibrous tissue without epithelial covering and very rarely showing caseation or specific tuberculous appearances. In the absence of clinical data it is almost impossible to prove the tuberculous aetiology of such cavities. They differ from emphysematous bullae in having thicker walls and being situated in the parenchyma of the lungs. Radiologically, too, the walls appear thicker than those of emphysematous bulla, and their outline is not absolutely regular and may present notches and bulges. Chemotherapy plays an important role in the formation of these cavities, and isoniazid is especially associated with their occurrence. Although the disease is apparently cured and the sputum negative at the time such cavities appear, spread may occur later and these authors therefore consider resection desirable as a prophylactic measure.

Pruvost *et al.*, on the other hand, although admitting the frequent relationship between treatment with streptomycin and isoniazid and the development of these bullous cavities, describe a case of pulmonary tuberculosis in which similar cavities developed while the patient was under observation over a period of 2 years during which he received no chemotherapy.

Simonin *et al.* report 2 further cases, in one of which they regarded the cavity as a tuberculous cavity sterilized by medical treatment and secondarily epithelized, whereas the other, in which the bullae appeared and disappeared rapidly, they considered to be an example of true bullous emphysema.

Bernou reports that among a number of tuberculous cavities which had been laid open on to the visceral pleura he was able to observe some whose lining was covered with caseous material and others with a clean lining, although in most cases this was nearly always covered with granulation tissue. In 2 patients with such cavities whose sputum was negative in 1947 there was no change in the radiological picture after 4 years. Now, after 7 years' observation, one cavity has become smaller, although its walls are thicker, a further cavity shows only stellate fibrosis, while a third has disappeared, the radiograph being almost completely clear. He agrees that these bullous cavities have occurred more frequently since the advent of streptomycin and especially of isoniazid, and emphasizes that the difficult diagnostic problem which they present is closely bound up with the

therapeutic problem: if they are purely emphysematous cysts they are best left alone but if they are tuberculous cavities, even with thin walls, they may well require resection. *G. M. Little*

363. **Enzymatic Debridement. Particular Reference to Trypsin and Desoxyribonuclease in the Control of Cough and Sputum Associated with Tuberculosis**
S. M. FARBER, R. D. GORMAN, D. A. WOOD, O. F. GRIMES, and S. L. PHARR. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 45–54, Jan., 1954. 4 figs., 15 refs.

In an effort to reduce the amount of cough and sputum in cases of pulmonary tuberculosis the authors have undertaken a clinical trial of various enzymes. Aerosols of trypsin, either alone or in combination with deoxyribonuclease, were given by inhalation to 26 patients at the San Francisco Hospital. The combination of the two enzymes was the more effective in reducing the amount of sputum and in decreasing its cellular content. However, the authors found that in a high proportion of cases toxic reactions to the enzymes occurred, mostly of a local nature and often including haemoptysis (71%); occasionally asthmatic attacks developed. They therefore recommend that these enzymes should not be used in aerosol form as a routine in the treatment of tuberculous patients. *J. R. Belcher*

EXTRA-RESPIRATORY TUBERCULOSIS

364. **Chemotherapy of Tuberculosis of Bones and Joints**
M. C. WILKINSON. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **36B**, 23–35, Feb., 1954. 6 figs., 20 refs.

In this paper from Black Notley Hospital, Braintree, Essex, the author attempts to assess the changes that have been made possible in the treatment of tuberculosis of bones and joints since the introduction of chemotherapy. Adult patients received streptomycin sulphate by intramuscular injection in a dosage of 1 g. daily for 90 days. Some patients also received a weekly injection of 200 mg. of streptomycin into the affected joint, but this practice was later abandoned because it appeared that with repeated trauma to the joint the synovitis tended to persist. PAS was combined with streptomycin only in those patients with associated pulmonary lesions. In a few cases isoniazid was given.

In patients with tuberculosis of the lumbar or thoracic spine no great difference was observed between those receiving streptomycin and those treated with rest in bed. In patients with tuberculosis of the hip or knee, however, the duration of preoperative treatment tended to be shorter in those receiving streptomycin. These findings suggested that streptomycin alone was not a major curative factor in the treatment of closed skeletal tuberculosis. Streptomycin had a marked effect, however, in patients undergoing curettage of a tuberculous spine with excision of an abscess, or excision of tuberculous tissue in the knee or hip. Of 26 children treated in this way for a tuberculous hip, 22 retained joint function; the same treatment applied to 4 adults was, however, a failure. Of 16 patients with tuberculosis of the knee, 13 recovered good knee function. In all the patients operated on who received streptomycin there was a considerable reduction in the period of treatment.

The author concludes that the use of streptomycin facilitates joint surgery. *Peter Ring*

365. **The Chemotherapy of Orthopaedic Tuberculosis**
F. H. STEVENSON. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **36B**, 5–22, Feb., 1954. 12 figs., bibliography.

The advantages and disadvantages of PAS, streptomycin, and isoniazid, alone or in combination with one another, in the treatment of all forms of tuberculosis are discussed. A clinical review of cases of bone and joint tuberculosis treated at the Royal National Orthopaedic Hospital, London, confirmed the value of streptomycin in promoting healing in the majority of cases of persistent tuberculous sinuses, failure usually being due to sequestra. In cases of closed bone and joint lesions a greater range of movement was obtained at the hip and knee in patients given an intramuscular injection of streptomycin than in patients treated without streptomycin, and the duration of treatment was reduced by 50%. [The relative failure of streptomycin in closed spinal lesions has been reported by Wilkinson (see Abstract 364).]

It is considered that a combination of streptomycin, PAS, and isoniazid is the chemotherapy of choice in bone and joint tuberculosis. In many patients, especially the young, this treatment alone may be sufficient. The role of surgery in resistant cases is discussed.

Peter Ring

366. **Possibilities and Limitations in the Treatment of Peripheral Tuberculous Lymphadenitis by Chemotherapy.** (Possibilités et limites du traitement des adénites tuberculeuses périphériques par les antibiotiques)
P. IMBERT, G. BERNARDIN, G. CHEVALLIER, P. VINCENT, and A. FREDERICH. *Journal de médecine de Lyon* [*J. Méd. Lyon*] **35**, 191–200, March 5, 1954. 2 refs.

At the Hôpital Renée-Sabran, Lyons, 105 cases of tuberculous lymphadenitis were treated with streptomycin, PAS, and isoniazid, the drugs being given either singly or in combination. Improvement definitely attributable to the treatment was noted in only 24 cases, but in another 20 it was thought that natural healing was probably accelerated. The favourable results were offset, however, by an increase in activity of the infection in 21 cases, with fever, toxaemia, and more intense adenitis, progressing to involvement of the skin and ulceration.

Streptomycin alone seemed to be the most useful drug, improvement being obtained in 13 of 39 cases so treated, with activation of the disease in 4 only. The combinations of streptomycin with isoniazid and of all three drugs given together were unsatisfactory, deterioration taking place in 4 of 9 patients treated with the former combination, and in 6 of 14 with the latter.

The authors conclude that chemotherapy has little place in the treatment of tuberculous adenitis, except in toxaemic cases, in cases with cutaneous ulceration, or as a cover for surgical removal. *D. Weitzman*

Venereal Diseases

367. **The Association of Lymphogranuloma Inguinale and Cancer**
R. RAINEY. *Surgery* [*Surgery*] **35**, 221–235, Feb., 1954. 14 figs., 31 refs.

It is well known that lymphogranuloma venereum causes stricture of the rectum, and in areas where this disease is common the Frei test should be carried out in all such cases. Only recently has it been suggested that there may be an association between lymphogranuloma venereum and rectal cancer, and in this paper 11 cases are reported from the Presbyterian and the Cook County Hospitals, Chicago, in which the former apparently predisposed to neoplastic degeneration. In 5 of the 11 cases the reaction to the Frei test, although previously positive, had become negative by the time the presence of carcinoma was diagnosed, and the author considers that this finding may form the basis of a diagnostic aid in the detection of latent carcinoma in lymphogranuloma venereum. He also stresses [rightly] the need for careful observation of all cases of anorectal lymphogranuloma. If the inflammatory process continues after correct chemotherapy and a preliminary colostomy then radical surgery is indicated. Colostomy *per se* does not remove the risk of development of anorectal neoplastic degeneration.

G. L. M. McElligott

368. **Intravenous Terramycin in the Treatment of Early Syphilis and Granuloma Inguinale**
E. M. C. DUNLOP and R. C. V. ROBINSON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 24–29, Jan., 1954. 14 refs.

In this paper from Johns Hopkins University and Hospital, Baltimore, the authors report their experience in the use of oxytetracycline given parenterally for the treatment of 4 confirmed cases of early syphilis and 4 of granuloma inguinale. Each patient was given 0·5 g. of oxytetracycline dissolved in 250 ml. of sterile water by intravenous drip over 10 to 15 minutes each day for 10 days. One patient complained of nausea during each treatment and had a nitritoid reaction during the first treatment, while 4 others complained of diarrhoea, one of whom also had nausea after the first injection.

The results of treatment in the 4 cases of syphilis, which were followed up for 90 to 220 days, are given. In 3 of the 4 patients the result of dark-field examination for treponemes was still positive after 24 hours, and in one patient it was positive after 48 hours; this patient subsequently relapsed, returning with a lesion from which treponemes were recovered after 90 days. Healing was slow, and generalized lymph-node enlargement persisted for 3 months in one patient. In 3 of the patients there was a tendency to reversal of serological findings, and one seronegative primary case, which became positive 13 days after treatment began, was again seronegative after 220 days. Of the 4 cases of granuloma inguinale, which were followed up for periods of 56 to 122 days, 2 were healed and 2 relapsed in 72 and 122 days respectively.

The authors conclude that the further use of oxytetracycline by intravenous infusion in the treatment of syphilis does not appear to be justified in view of the difficulty of administration and the proved efficacy of other modes of treatment, and that for the treatment of granuloma inguinale the intravenous administration of oxytetracycline in the dosage used does not seem to be as effective as other proved modes of treatment, including the oral administration of this drug.

Benjamin Schwartz

369. **Oxytetracycline Intramuscular in the Treatment of Gonorrhea**
B. SEID. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 330–332, March, 1954. 7 refs.

370. **The Treatment of Urethritis with a Combination of Aureomycin and Sulphonamides.** (Essai de traitement des urétrites par une association auréomycine–sulfamides à faibles doses)
B. PIGUET and L. FOERSTER. *Prophylaxie sanitaire et morale* [*Proph. sanit. morale*] **26**, 37–42, Feb., 1954.

Writing from the Institut Alfred Fournier, Paris, the authors discuss their method of treatment of urethritis with aureomycin and sulphonamides in small doses, the drugs being given in capsules each containing 0·125 g. of aureomycin combined with 0·167 g. each of sulphadiazine, sulphamerazine, and sulphadimerazine. The patient is given 4 or 6 of these capsules in 24 hours, 8 in 48 hours, or 12 in 72 hours.

The results of treatment, which was well tolerated in all the 71 cases reviewed, are tabulated and were as follows. (1) Of 40 cases of acute gonorrhoea, 23 were completely cured, 5 were improved (in that gonococci were no longer found but some discharge persisted), in 7 cases the treatment failed, and 5 were not followed up. The failures all occurred in cases given only 4 or 6 capsules, that is when the total dose of aureomycin was less than 1 g. (2) In cases of chronic gonorrhoea receiving either 8 or 12 capsules treatment was unsuccessful. In one of these cases the causal organism was shown to be resistant to penicillin, streptomycin, chloramphenicol, and sulphonamides. (3) Of 12 cases of acute non-gonococcal urethritis, 3 were cured, 3 improved, and 6 failed to respond. (4) Of 17 cases of chronic non-gonococcal urethritis, 5 were cured, 6 improved, 4 were not benefited, and 2 were not followed up.

The authors conclude that although the results of treatment in cases of chronic gonorrhoea and non-gonococcal urethritis were variable, the combination of aureomycin and sulphonamides for the treatment of

acute gonorrhoea was as effective as other methods, while the dose of aureomycin was only 50% of that usually employed. *Benjamin Schwartz*

SYPHILIS

371. **A New Aqueous Treponemal Antigen in the Serological Investigation of Syphilis by Means of the Complement-fixation Reaction.** (Über ein neues wässriges Spirochätenantigen zum serologischen Luesnachweis mittels der Komplementbindungsreaktion)
F. FÜHNER and W. GAEHTGENS. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **138**, 573–580, 1954. 10 refs.

The authors describe their experience at the Institute of Hygiene in Hamburg with the " pallida reaction ", a complement-fixation test for the presence in the serum of antibodies to treponemal protein in which an antigen prepared from a suspension of the Reiter strain of *Treponema pallidum*, cultured anaerobically, is used. Details of the technique are given. Some 8,700 sera were subjected to six parallel serological tests; the pallida reaction gave the highest number of positive results (1,229), followed by the Kolmer reaction (948) and the cardiolipin Wassermann reaction (748). The specificity of a positive result was judged from the over-all picture given by the six tests and from the clinical impression of the case.

It is stated that a positive pallida reaction, persisting on repetition, may occur in the presence of negative reactions to the anti-lipid tests in early primary infections, in neurosyphilis, and in latent syphilis. It is the last of the serological reactions to become negative on cure, remaining positive as long as the Nelson test. A persistent isolated positive reaction, strong or medium, to the cardiolipin or Kolmer test in the presence of a negative pallida reaction may mean that a non-specific anti-lipid antibody persists after the specific antibody to treponemal protein has disappeared. In the offspring of treated syphilitic mothers the pallida reaction was occasionally negative in the presence of positive reactions to the cardiolipin tests—possibly owing to transplacental transfer of antibody.

It is suggested that as the anti-lipid and anti-protein antibodies may be of different biological significance, the determination and comparison of their quantitative titres may prove of value in prognosis. *Ferdinand Hillman*

372. **The Intradermal Reaction to Suspensions of Formolized Pathogenic Treponemes (Nichols strain).** (L'intradermo-réaction aux suspensions de tréponèmes pathogènes (souche Nichols) formolés)
J. GATÉ, J. THIVOLET, A. SIMERAY, and M. ROLLAND. *Annales de médecine* [*Ann. Méd.*] **54**, 633–651, 1953. 5 figs., 38 refs.

The authors, working at the Faculty of Medicine, Lyons, have prepared the antigen for an intradermal test for the presence of syphilis by extracting the testes of rabbits infected with the Nichols strain of *Treponema pallidum*. The testes, which are removed when the stage of early acute orchitis is reached, are sliced and shaken for several hours on a Kahn shaker with 10 to 20 ml. of sterile saline solution, and the suspension centrifuged slowly to deposit gross debris. To the supernatant fluid 1% formalin is added to kill the organisms, which are then separated by centrifuging three times at 10,000 r.p.m. The deposit is suspended in 0·05% formolized saline, the aim being to achieve a density of 100,000 treponemes per c.mm. In carrying out the test, 0·2 ml. of the suspension is injected intradermally into the deltoid region and the reaction read on the fourth day. A transient erythema may develop in the first 48 hours, but disappears on the third day. Reactions vary in intensity from +, a slightly infiltrated papule 3 to 5 mm. in diameter, to ++++, a papule more than 2 cm. in diameter with an areola and vesicle.

The reaction is thought to be highly specific. No positive reactions were seen in 105 non-syphilitic patients, most of whom were suffering from skin diseases. Sensitivity to the test appears to develop at the end of the secondary stage and in latency. Out of 211 known cases of syphilis examined, 10 patients with primary syphilis and 14 out of 15 with secondary syphilis gave negative results; in the one secondary case which gave a positive reaction there was a varioliform eruption which resembled malignant syphilis. In 16 out of 28 cases of latent syphilis the skin tests were all positive, as they were also in cases of late syphilis, 11 patients with tertiary skin lesions, 7 with cardiovascular lesions, and 13 with stigmata of congenital syphilis all giving a positive reaction to the skin test. However, only 11 out of 22 patients with neurosyphilis showed positive reactions; it was noted that in cases giving a negative reaction, a positive reaction may develop after treatment, and it is suggested that this reversal might possibly be used as an indication of the efficacy of treatment. Out of 58 patients with treated syphilis in whom positive serological reactions had been converted to negative, 19 gave a positive skin reaction compared with 34 out of 47 treated patients in whom the serological reaction had not been converted.

Attempts at chemical fractionation of the treponemal antigen were made. The results of preliminary work suggested that the skin reaction is more closely linked to the protein fraction than to the lipid or carbohydrate components. *A. E. Wilkinson*

373. **Syphilis in Pregnancy**
C. BERLIN and C. MEYROVITZ. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 28–30, March, 1954. 15 refs.

During the eight years, 1944–52, routine serologic blood examination of 37,540 pregnant women revealed 153 positive or doubtful reactions.

Specific treatment was administered to 111 expectant mothers in 127 pregnancies: 26 women had early symptomatic or latent syphilis (of less than 4 years' duration); 57 had late symptomatic or latent syphilis; 8 had congenital syphilis; in 11 the stage could not be ascertained; in 9 there was only questionable evidence of syphilis.

In 25 cases the patients received arsphenamine and bismuth therapy, in 12 metal chemotherapy concurrently with penicillin, and in 80 penicillin alone. Aqueous penicillin 3-hourly, totalling 4·8 million units, was given to 56 patients in hospital, and procaine penicillin 600,000 units daily for 10 days was given to 52 outpatients. In most cases syphilotherapy was started in the second half of the pregnancy. There were 8 treatment failures, 4 possibly and 4 probably due to syphilis. They all occurred in patients with early syphilis, after treatment with metal chemotherapy (4), penicillin (3), and chemotherapy with penicillin (1).

In addition to the important advantages of convenience of application, almost complete lack of toxicity, and brevity of treatment, penicillin given to an expectant mother has superior therapeutic effects and offers greater safety for the child.—[Authors' summary.]

374. **Endemic Syphilis in a South African Coloured Community**

W. N. TAYLOR. *South African Medical Journal* [*S. Afr. med. J.*] **28**, 176–178, Feb. 27, 1954. 6 refs.

It is increasingly recognized that there are forms of syphilis which are neither venereal nor congenital in origin—for example, the endemic form occurring in the Balkan countries, " bejel " among the Arabs, and " novjera " in Southern Rhodesia and Bechuanaland. It has been suggested that these non-venereal forms are distinct disease entities although they are caused by the same organism as venereal syphilis—that is, they are diseases of the same order as pinta and yaws.

The present author, who observed a number of cases of non-venereal syphilis in a town in the Eastern Cape Province, South Africa, states that the conditions which are conducive to the development of the endemic form of syphilis are: (1) a high proportion of cases of syphilis of any kind in the general population; and (2) poor and insanitary living conditions. Coloured people—that is, people of mixed blood—are more often affected than the Bantu. Endemic syphilis is principally a disease of childhood and appears to spread from family to family. The lesions do not differ from those of venereally-acquired syphilis, though the primary chancre is not seen. The commonest lesions are condylomata of the anus or vulva, though a papular type of rash is relatively common. The author did not observe any lesions of the mucous membranes, teeth, or bones. External lesions respond rapidly to administration of arsenic or penicillin; they may clear up spontaneously after a few months without treatment.

Neville Mascall

375. **Oxytetracycline Intramuscular in the Treatment of Yaws (Pian)**

E. H. LOUGHLIN, A. A. JOSEPH, and F. DUVALIER. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 155–164, Feb., 1954. 11 figs., 3 refs.

At the Yaws Investigation Center, Gressier, Haiti, 120 West Indian patients, 108 with early and 12 with late yaws, were treated with oxytetracycline (" terramycin ") given intramuscularly. For adults and children over 10 years of age the dosage was 250 mg. once daily for 5 days, for children between 5 and 10 years 200 mg., and for children under 5 years 150 mg. daily over the same time. No systemic or local toxic reactions were observed.

The results of this treatment were excellent and in some cases spectacular. *Treponema pertenue* disappeared from the early lesions within 24 to 72 hours. In 50 cases with primary lesions, these had healed by the fifth day in all but 14 which were heavily contaminated with bacteria, but these latter cases responded to additional oxytetracycline given locally. Secondary lesions likewise healed readily, and the disabling pain in plantar lesions was greatly reduced. Late manifestations, such as gangosa, were arrested, while deforming osteoperiostitis, tenosynovitis, and dactylitis regressed. Recurrence was noted in 6 patients, but in 4 of these fresh primary lesions appeared on their return to an area of endemic yaws; these cases were considered to be due to reinfection.

The authors comment particularly on the great improvement in morale of the community, as evidenced by the willingness of the patients to return for follow-up examinations. Many of these cases had been previously treated with " one-shot " procaine penicillin.

R. R. Willcox

376. **Time–Dosage Relationship in the Treatment of Treponemal Diseases with a New Combination of Three Penicillin Salts. Laboratory and Clinical Basis for Effective Therapy**

C. R. REIN, F. H. BUCKWALTER, C. H. MANN, S. E. LANDY, and S. FLAX. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **21**, 435–446, Dec., 1953. 2 figs., 5 refs.

The trial of a new combination of three penicillin salts (" panbiotic ") in the treatment of treponema infections is described in this paper from New York University. The combination provided 300,000 units each of potassium benzylpenicillin and of procaine benzylpenicillin and 600,000 units of N:N′-dibenzylethylene diamine dipenicillin G as an aqueous suspension in each 2 ml. The object was to achieve an immediate high blood concentration of penicillin, this being maintained for at least 36 hours by the procaine compound and thereafter for about 15 days by the relative insolubility of the third component. In a total of 94 patients treated there was little pain or tenderness after intramuscular injection and few urticarial or other reactions. The preparation was stable and easily administered. An initial blood level of 4 units per ml. was rapidly obtained, and a concentration of 0·04 unit per ml. persisted for 15 days.

It is claimed that this drug combination is likely to be of value in cases of yaws or pinta in which there is much secondary infection, and particularly useful in countries where patients have to be treated by a single-injection method.

(In the discussion which followed it was suggested that panbiotic might be used in the treatment of acne vulgaris, an injection every two weeks controlling pustular infection.) *Robert Lees*

Tropical Medicine

377. **Treatment and Prevention of Kwashiorkor**
R. F. A. DEAN. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **9**, 767–783, 1953. 6 figs., 3 refs.

From his experience in the treatment of kwashiorkor and his observation of the diets of natives of East Africa, the author believes that a diet rich in protein is the first essential in both treatment and prevention of this disease. Meat, fish, and milk are scarce and expensive locally. To obtain 1,200 Calories a day a child would have to consume 1,500 grammes of sweet potatoes and plantains, and while a healthy child can do this a sick child can seldom be persuaded to take more than 500 to 600 grammes a day. Infectious diseases make additional demands on the metabolism while reducing the appetite. In treatment the author gives as much protein as possible, supplemented with vitamins, particularly vitamin B_{12}, which accelerates growth in convalescents. Fat is not well tolerated. A few cases are briefly described in which a diet of milk and soy bean meal was effective. Sweet banana has proved of value as a source of carbohydrate and as a vehicle for milk and soy bean flour.

Discussing prevention the author states that the prospects of improving the local supply of animal protein are not good. On the other hand, good vegetable protein is available in the form of soy beans and groundnuts. In his view attention should be paid to the value of sunflower seed. Sunflowers are grown on a big scale in Uganda and the seed yields an oil of high commercial value, leaving a meal containing 35% protein which is rich in methionine. *William Hughes*

378. **The Control of Cholera Epidemics in India by Compulsory Anti-cholera Inoculation of Pilgrims before Travelling through Infected Districts to Attend Fairs**
L. ROGERS. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **48**, 42–49, Jan., 1954. 10 refs.

This is the latest chapter in the distinguished author's statistical studies of cholera in India over the last 86 years. He has shown previously that an exceptionally high incidence of cholera in any year could be related to serious deficiencies in the monsoon rains in the preceding season (with subsequent malnutrition or famine) or to epidemics spread by pilgrims attending the 12-yearly Kumbh Fairs at Allahabad and Hardwar.

The official figures for deaths from cholera in India for the 12 years 1940–51 show that, apart from a rise in the years 1941–5 (which the author attributes to malnutrition resulting from war scarcities and high prices), mortality has remained steady at a comparatively low level (0·2 to 0·7 per 1,000), while the average of 0·64 per 1,000 is less than for any previous decade. He attributes this to the increasing insistence on the compulsory inoculation of the 20,000,000-odd pilgrims who annually travel long distances through cholera-infected districts to visit religious fairs and festivals, and points out that for the first time in history a major epidemic failed to follow the Kumbh fairs at Allahabad in 1942 and at Hardwar in 1950. During this decade, however, there was no marked annual variation in rainfall, and the new methods of control remain to be tested in a year following failure of the monsoon rains. *Clement Chesterman*

379. **Milk, *p*-Aminobenzoate, and Malaria of Rats and Monkeys**
F. HAWKING. *British Medical Journal* [*Brit. med. J.*] **1**, 425–429, Feb. 20, 1954. 4 figs., 17 refs.

When Maegraith *et al.* reported (*Brit. med. J.*, 1952, **2**, 1382) that a milk diet prevented the development of *Plasmodium berghei* in rats, the present author pointed out (*Brit. med. J.*, 1953, **1**, 1201) that supplementation of the milk diet with *p*-aminobenzoate permits the normal development of various species of plasmodia in the rat and monkey.

In the well-designed series of experiments here reported from the National Institute for Medical Research, London, the author has confirmed that the missing growth factor in a milk diet is *p*-aminobenzoate. When this substance was given orally or parenterally to monkeys or adult rats (weighing at least 200 g.) maintained on a milk diet, *P. berghei* infection developed as it did in control animals on a stock diet. The concentration of *p*-aminobenzoate in milk necessary to permit growth of the plasmodium was about 1 in 40,000, and an equimolar concentration (1 in 10,000) of pteroylglutamic (folic) acid had the same effect. The two substances are obviously interchangeable, but it is not clear which is changed into the other in the course of metabolism. It was found that if the milk in the diet was allowed to sour, plasmodium infection sometimes developed, probably because of the elaboration of *p*-aminobenzoate during the process of souring. (An incidental finding of interest was that when chloramphenicol was given to control diarrhoea caused by the milk diet, the malarial infection developed. This was disconcerting until it was learned that *p*-aminobenzoate is one of the degradation products of chloramphenicol in intestinal putrefaction.) The addition of methionine, vitamin B_{12}, or *p*-hydroxybenzoate to the milk did not reverse the suppressive action of the diet.

In a further series of experiments it was shown that breast-fed young rats failed to develop infection with *P. berghei*, and breast-fed baby monkeys similarly failed to develop *P. knowlesi* infection. The author was able to show that *p*-aminobenzoate was the missing factor in the diet in both cases, since growth of the plasmodium could be promoted by injecting *p*-aminobenzoate parenterally into the young animals, by adding it to the milk directly, or introducing it indirectly by applying it to the mother's nipples or injecting it into the mother.

Discussing the significance of his findings, the author points to the relative immunity to malaria of infants in

hyperendemic regions; this has been thought to be due to immunity inherited or acquired from the mother, but in the light of the present findings it now seems possible that their insusceptibility is due to their exclusive milk diet, since most of these infants are wholly breast-fed to the age of about 5 months. In view of the biological antagonism between *p*-aminobenzoate and the sulphonamides it is interesting to note that investigations made so far show that the development of several types of plasmodia known to be sensitive to the sulphonamides can be inhibited by a milk diet. The author's findings also help to explain the antimalarial action of proguanil and pyrimethamine, which is probably due to their interference with the utilization of *p*-aminobenzoate or some derivative like folic acid. One curious discrepancy was noted, namely, that the amount of *p*-aminobenzoate necessary to reverse the inhibitory action of the milk diet in rats was about 20 mg. per kg. body weight per day—an amount much more than one could reasonably expect to find in the normal stock diet.

William Hughes

380. **Three Early Cases of Rhodesian Sleeping Sickness Treated with Pentamidine Isethionate**

M. GELFAND and W. D. ALVES. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **48**, 146–149, March, 1954. 8 refs.

381. **The Treatment of Intestinal Amebiasis with Fumagillin (Fugillin)**

E. L. MACQUIDDY. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 178–183, Feb., 1954. 8 refs.

The author has used fumagillin, a substance prepared from *Aspergillus fumigatus*, in the treatment of 82 cases of intestinal amoebiasis, 60 of which had previously been treated unsuccessfully with other drugs. The cases were divided into four groups of increasing grades of severity. Of 10 cases in Grade I given 200 to 400 mg. (800 mg. in 2 cases) of fumagillin by mouth in capsules, 8 showed definite improvement. Of 37 in Grade II receiving 140 to 800 mg., there was improvement in 32, one was lost to follow-up, and 4 showed no benefit. Of 23 in Grade III receiving 100 to 1,600 mg., 18 showed improvement, while in 5 the results were inconclusive. Of 12 patients in Grade IV given 100 to 1,200 mg., 10 appeared to benefit. A follow-up examination after 3 months has so far been possible in only 32 cases, but in 29 of these the stools were negative for amoebae.

When this treatment was begun (in April, 1952) twenty 40-mg. capsules were given over 10 days, but as a number of patients complained of severe abdominal cramps, dizziness, nausea, nervousness, and a vesicular rash on the hands and feet, the dose was decreased to 20 mg. twice daily and then further to 10 mg. twice daily for 10 days. With the reduction in dose the number of toxic reactions decreased also.

The author also describes certain interesting radiological appearances seen in cases of amoebiasis, consisting in a fine serration of the mucosal pattern of the bowel, which differed from that seen in ulcerative colitis.

R. R. Willcox

382. **Further Trial of Aureomycin in the Treatment of Cholera**

S. C. SEAL, M. M. GHOSH, and S. C. GHOSAL. *British Medical Journal* [*Brit. med. J.*] **1**, 740–742, March 27, 1954. 4 refs.

The value of aureomycin in the treatment of cases of cholera was studied during an epidemic of the disease in Calcutta in 1951. The results obtained in 50 patients given aureomycin by mouth and saline intravenously were compared with those obtained in 35 who received sulphaguanidine with saline intravenously and in 35 given saline only. The three groups were comparable, except that the group receiving aureomycin was treated earlier than the two control groups. One capsule (250 mg.) of aureomycin was given every 3 hours to an average total in severe cases of 6·65 g. and in mild cases of 4·9 g. No untoward effect directly referable to the drug was observed. The total dose of sulphaguanidine averaged 25 g. All patients in a state of dehydration and collapse on admission received saline, glucose, and alkalis intravenously.

Of the patients treated with aureomycin, 7 died, 2 of them shortly after admission; 5 patients died in each of the other two groups; there was thus little difference in mortality between the three groups (approximately 14%). The duration respectively of the acute stage of the disease, suppression of urine, and excretion of vibrios was significantly lower in the patients given aureomycin than in the others. The incidence of complications was, however, lowest in the group receiving saline only.

The authors consider that treatment with vibriocidal drugs is indicated only in the earliest stages of cholera and may be harmful once dehydration and collapse have set in owing to liberation of endotoxin.

W. H. Horner Andrews

383. **The Treatment of Ascariasis and Ancylostomiasis with Hetrazan (Diethylcarbamazine)**

M. H. GHANEM. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **48**, 73–76, Jan., 1954. 7 refs.

" Hetrazan " (diethylcarbamazine) was administered to 138 hospital in-patients in Alexandria who were found to be infested with *Ascaris lumbricoides* or *Ancylostoma duodenale*, or both. Two dosage schedules were used. (1) A single course of 10 mg. per kg. body weight in 3 doses daily for 3 days cured 43 (41%) of 104 cases of ascariasis and 4 (13%) of 31 of ancylostomiasis; the course was repeated up to five times if necessary, but even then the rate of cure was only 89% for ascariasis and 58% for ancylostomiasis. (2) Slightly better results were obtained with a dose of 25 mg. per kg. given similarly, but gastrointestinal side-effects were more marked and bilharzial dysentery was activated in 4 out of 28 cases.

The author considers that because of its low toxicity hetrazan might be of value for the treatment of ascariasis in anaemic or seriously ill patients and in children, but that it is less useful for mass treatment on account of the time and cost involved, while it is much less effective against ancylostomiasis.

Clement Chesterman

Nutrition and Metabolism

384. **Carbohydrate Metabolism in Ascorbic Acid Deficiency**
H. BACCHUS and M. M. HEIFFER. *American Journal of Physiology* [*Amer. J. Physiol.*] **176**, 262–266, Feb., 1954. 3 figs., 21 refs.

A disturbance of carbohydrate metabolism in association with ascorbic acid deficiency has been often demonstrated. The diminished glucose tolerance which occurs has been thought to be related not to increased adrenaline content of the adrenal glands, but rather to a decrease in the insulin content of the pancreas; it has also been suggested that adrenal cortical hyperactivity may account for the scorbutic disturbance in carbohydrate metabolism.

The present experiments, carried out at George Washington University, Washington, D.C., confirmed that the insulin tolerance of ascorbic-acid-depleted guinea-pigs is diminished and that a progressive resistance to the hypoglycaemic action of insulin accompanies ascorbic acid deficiency. In order to ascertain whether the disturbance was related to adrenal hyperactivity glucose–insulin tolerance tests were repeated on adrenalectomized guinea-pigs and on controls deprived of ascorbic acid. Both the adrenalectomized and the intact animals, however, were found to be resistant to the hypoglycaemic action of insulin. While the exact mechanism still remains obscure, these experiments seem to indicate that the disturbance of carbohydrate metabolism occurring in ascorbic acid deficiency is probably not due to diminished insulin secretion—since exogenous insulin failed to correct it; nor to adrenal hyperactivity—since insulin resistance was present even in the adrenalectomized animals. *Z. A. Leitner*

385. **The Effects of Vitamin Deficiencies on Some Physiological Factors of Importance in Resistance to Infection. I. Niacin–Tryptophane Deficiency**
K. WERTMAN, L. W. SMITH, and W. M. O'LEARY. *Journal of Immunology* [*J. Immunol.*] **72**, 196–202, March, 1954. 40 refs.

386. **Effect of Phenylbutazone on Uric Acid Metabolism**
R. M. MASON. *British Medical Journal* [*Brit. med. J.*] **1**, 788–792, April 3, 1954. 5 figs., 10 refs.

It has been claimed that phenylbutazone causes a striking diminution in the serum uric acid level in acute gout. The author has studied the effect of the drug in 5 cases of acute gout at Chase Farm Hospital, Enfield, Middlesex. He states that a specific effect on uric acid metabolism and on acute gout would be unique.

In the first case administration of 600 mg. daily of phenylbutazone resulted in a fall in the blood uric acid level from 11·6 mg. to 4·3 mg. per 100 ml. by the tenth day; there was excess excretion of uric acid amounting to 1,485 mg. during the 10 days. In the second case the serum uric acid level fell from 4·7 mg. to 3·5 mg. per 100 ml. in 7 days, the excess uric acid excreted being 620 mg. In the third case the total excess of uric acid excreted was 2,254 mg. in 7 days, but the serum level fell only from 5·4 mg. to 4·8 mg. per 100 ml. The plasma uric acid level did not fall in the fourth case, in which, moreover, an actual retention of 365 mg. uric acid was observed; there was appreciable water retention in this case. The fifth patient had Paget's disease, but during the first week of phenylbutazone therapy the plasma uric acid level fell from 4·9 to 2·6 mg. per 100 ml. and the uric acid excreted amounted to 686 mg.

In the second, third, and fifth cases the fall in the uric acid concentration in the serum was roughly equivalent to the amount excreted, assuming equal distribution in the body water, but in the first case the fall in the serum level was much greater than could be accounted for by the urinary excretion. It is suggested that the variable results were due to the water-retaining and uricosuric properties of the drug, and that a direct effect on uric acid metabolism has not been proved. *C. L. Cope*

387. **A Clinical Study of 136 Cases of Gout in the Male.** (Étude clinique de 136 cas de goutte masculine)
J. SÉRANE and R. BONNIOT. *Presse médicale* [*Presse méd.*] **62**, 507–508, April 3, 1954. 23 refs.

388. **Iron Metabolism in Steatorrhea. The Use of Radioactive Iron in Studies of Absorption and Utilization**
J. BADENOCH and S. T. CALLENDER. *Blood* [*Blood*] **9**, 123–133, Feb., 1954. 6 figs., 9 refs.

At the Radcliffe Infirmary, Oxford, the absorption of iron was studied in 16 patients with defective fat absorption and in 15 control patients without steatorrhoea by means of an oral test dose of 200 mg. of a ferrous sulphate mixture containing 40 mg. of iron to which was added 5 μc. of radioactive iron (^{59}Fe), the radioactivity being measured in 20-ml. samples of blood every 3 or 4 days until a constant level was reached. In addition the faeces were examined for unabsorbed iron, and the intravenous iron utilization test described by Huff *et al.* (*Acta haemat.* (*Basel*), 1952, **7**, 129) was also carried out.

The results, which are tabulated, showed that in the 13 patients with idiopathic steatorrhoea iron absorption was low compared with that in the control subjects, although utilization was rapid when iron was given by intravenous injection. One patient with steatorrhoea associated with gastroenterostomy showed good absorption of orally administered iron, while one of the control patients with normal fat absorption absorbed iron poorly.

The authors conclude that the iron-deficiency anaemia of steatorrhoea is primarily due to poor absorption, although there is some evidence to suggest that this is not the only factor in its causation. *J. M. French*

Gastroenterology

389. **A Biological Study of the External Secretion of the Pancreas. Spontaneous Tryptic Activity.** (Étude biologique de la sécrétion pancréatique externe. L'activité trypsique spontanée)
A. MANGEOT, C. MARCY, and L. LÉGER. *Annales de médecine* [*Ann. Méd.*] **54**, 604–618, 1953. 1 fig., 7 refs.

The authors have had the opportunity during surgical operations at the Salpêtrière Hospital, Paris, to obtain pancreatic juice by direct catheterization of the pancreatic duct. The juice thus collected, free from contamination by the duodenal contents, was subjected to chemical and biological analysis. In a number of cases it was possible to leave the catheter *in situ* for several days, so permitting study of the variations in secretion of the juice.

In general, the physical and chemical properties of the juice conformed well to the classic text-book description. Secretion, estimated at hourly intervals, was found to be lowest on the day of operation (0·1 to 3 ml. per hour), rising steeply by the third day (0·7 to 33 ml. per hour). The chloride content varied inversely with the bicarbonate content, the latter increasing as collection was continued and the chloride content falling; the sum total of the ions, expressed in mEq., remained, however, relatively constant.

Study of the enzymatic action of the pancreatic juice showed that its lipolytic action tended to increase steadily in the days after the operation. The most interesting and surprising result was the finding in every case of trypsin in the active form, instead of as trypsinogen as has been generally reported hitherto. The activity of the trypsin was inversely proportional to that of lipase and declined rapidly during the period of observation, being highest during the first 24 hours and entirely absent by the fifth day; it could not be restored by the addition of calcium or magnesium salts or fresh juice. This finding, which has been reported before but usually only in single cases, is discussed at some length. The authors suggest [but apparently without much conviction] that a post-operative discharge of acetylcholine may be responsible for the secretion of active juice. *L. H. Worth*

390. **The Effect of Drug-induced Hypermotility on the Gastrointestinal Tract of Dogs**
H. C. MOELLER and J. B. KIRSNER. *Gastroenterology* [*Gastroenterology*] **26**, 303–311, Feb., 1954. 2 figs., 15 refs.

Experiments were carried out at the University of Chicago on dogs to investigate the possibility that prolonged hyperactivity and spasm of the bowel might be important factors in the aetiology of ulcerative colitis. Large doses of pituitary extract given for 30 days and of castor oil or magnesium sulphate given for 204 days produced no demonstrable gross or microscopic changes in the intestine. Severe changes in the rectal mucosa were, however, found in dogs given neostigmine, carbachol, or " amechol " (methacholine) daily for 30, 50, and 14 days respectively. The microscopical changes included epithelial necrosis and intramucosal haemorrhage. The effect of amechol was further studied in 27 dogs by giving daily subcutaneous injections of 2 to 4 mg. per kg. body weight suspended in a beeswax–peanut-oil mixture for from 6 to 770 days. Symptoms of parasympathetic stimulation appeared initially and severe diarrhoea occurred within 48 hours of the first injection. After several months of such injections, the animals' general condition being maintained by careful feeding, proctoscopy showed hyperaemia, haemorrhage, and a friable mucosa with punctate ulceration. This acute or subacute ulcerative proctitis with bloody diarrhoea cleared up quickly when the drug was discontinued. Erosions and ulceration in the antrum of the stomach were found in 14 of the dogs. Superficial erosions and necrosis were common in the small intestine and colon. There were no ulcers in the colon, but submucosal haemorrhage was found on the crests of the submucosal folds. These parasympathomimetic drugs produced a condition resembling mild ulcerative colitis in man, but chronic colitis was not observed.

In conjunction with the reports of other workers on the state of the distal colon in normal human subjects given such substances, in patients with irritable colon and diarrhoea, and in those with ulcerative colitis, these results support the possibility that parasympathetic overstimulation and hyperactivity of the colon are concerned in the aetiology and chronicity of human ulcerative colitis. *Derek R. Wood*

OESOPHAGUS

391. **Observations on the Normal Oesophagus and Cardia**
A. C. DORNHORST, K. HARRISON, and J. W. PIERCE. *Lancet* [*Lancet*] **1**, 695–698, April 3, 1954. 9 figs., 1 ref.

The behaviour of the normal oesophagus and cardia was studied in 6 healthy volunteers at St. Thomas's Hospital, London, a technique being employed in which radiography was carried out simultaneously with measurement of intra-oesophageal pressure. Pressure was measured with a manometer through a mercury-tipped polythene tube, the recording position being thus easily identified on the radiograph. An electrical link between the pressure record and the *x*-ray tube provided precise timing of the radiograph.

The authors state that the normal oesophageal propulsive wave is of characteristic form, taking about 4 seconds to complete, with peak pressure between 20 and 50 mm. Hg, and is usually initiated by a pharyngeal swallow. There is no relaxation preceding the contraction. In the immediate vicinity of the cardia the con-

traction becomes less forceful and lingers up to 20 seconds. The cardia itself, from the point of view of function, is a localized region extending over not more than 5 mm. This region has the characteristics of a valve—that is, it offers very small resistance to forward passage, but resists retrograde flow in spite of large inverse pressures. The valvular mechanism appears to be formed by the action of the muscularis mucosae on the mucosa. While the large inverse pressures to which the cardia may be subjected involve contraction of the diaphragm, there is evidence that this contraction does not itself occlude the oesophagus. *Joseph Parness*

392. **The Oesophageal Lesion in Scleroderma**
A. C. DORNHORST, J. W. PIERCE, and I. W. WHIMSTER. *Lancet* [*Lancet*] **1**, 698–699, April 3, 1954. 2 figs., 1 ref.

It is well known that in symmetrical progressive scleroderma (sclerodactyly), oesophageal lesions may produce dysphagia. It is less well known that in this condition a disorder of oesophageal function is often demonstrable when the patient is unaware of any difficulty in swallowing.

Using the method described in Abstract 391 the authors examined 6 consecutive patients suffering from sclerodactyly, none of whom had complained of dysphagia. In all the patients the propulsive waves failed to continue normally into the lower half of the oesophagus although the upper half contracted with normal vigour. The weakness of the lower oesophagus was observed radiologically when the patient swallowed while in the supine, slightly head-down position (anti-gravity swallowing). These findings and the microscopic appearance of necropsy material from 2 further cases indicate that the essential lesion is simple muscle weakness and wasting in the lower half of the oesophagus. The authors conclude that oesophageal disorder in sclerodactyly is common. *Joseph Parness*

STOMACH AND DUODENUM

393. **The Achlorhydric Patient with Dyspepsia**
B. F. SWYNNERTON and N. C. TANNER. *British Medical Journal* [*Brit. med. J.*] **1**, 546–552, March 6, 1954. 3 figs., 15 refs.

Achlorhydria was detected in 403 patients with dyspepsia admitted to St. James's Hospital, London, between 1940 and 1946. On gastroscopy advanced atrophy of the gastric mucosa was found in 113 and atrophic gastritis and early atrophic changes in 126. In the present paper these 239 cases are discussed, and the findings at a follow-up investigation 5 to 10 years after the patients were first seen are described. The ratio of males to females was 4:3 and the incidence increased with age, being highest in patients aged 50 years. Acute erosions, acute, subacute, or chronic ulcers, or ulcer scars were found in a high proportion of patients, over 90% of whom complained of upper abdominal pain or discomfort. Symptoms, which in some cases had been present for over 20 years, were often related to food and accompanied by haemorrhage from a definite peptic ulcer or from erosion of a vessel lying just beneath the atrophic mucosa. In some cases the symptoms suggested gall-bladder dyspepsia. Loss of weight, nausea and vomiting, and anorexia were present in 20%, but constipation and diarrhoea were uncommon. Associated disorders included gastric adenomata, gall-bladder disease, tertiary syphilis, and chronic infection of the respiratory tract.

Only 16 of the 239 patients were untraced. Of the patients with advanced atrophy, 22 died without developing gastric carcinoma, whereas 38 of the patients with early atrophic changes died, 4 of them from carcinoma of the stomach. There were no obvious common aetiological factors. Of the patients who were still alive at the time of the follow-up, 25% remained free from symptoms, while 42% continued to suffer from troublesome discomfort.

The treatment of atrophic gastritis is discussed, administration of dilute hydrochloric acid being advised, though the authors found that the majority of patients continued to take alkalis. *K. Gurling*

394. **Anaemia Associated with Diaphragmatic Herniation of the Stomach in the Adult.** (À propos des formes anémiques des hernies diaphragmatiques de l'estomac chez l'adulte)
P. HILLEMAND, P. ISCH-WALL, R. WATTEBLED, and J. E. VARELA. *Presse médicale* [*Presse méd.*] **62**, 223–225, Feb. 13, 1954. 2 figs., bibliography.

Anaemia, which is a rare complication of diaphragmatic hernia of the stomach through the oesophageal hiatus, may be discovered only when the patient is examined because of a complaint of gastrointestinal symptoms or it may be the main symptom. It is usually hypochromic in type, but may occasionally be normochromic. Of 280 patients with diaphragmatic hernia seen during a 3-year period, only 4 had anaemia. From a study of the pathogenesis the authors believe that the anaemia is in some cases the result of a haemorrhagic oesophagitis caused by reflux of gastric contents. Such a lesion was recognized by oesophagoscopy in 4 of 9 cases which they have personally observed. In other cases there was evidence of hypothyroidism with a low basal metabolic rate. *P. C. Reynell*

395. **Perigastritis Deformans following Diseases of the Left Lung and Pleura.** (Perigastritis deformans nach linksseitigen Lungen- und Pleuraerkrankungen)
E. MINDER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **84**, 189–193, Feb. 6, 1954. 8 figs., 33 refs.

The syndrome known as perigastritis deformans was first described by a number of authors about the year 1910, though not then under that name. It is one of the conditions which should be considered in the differential diagnosis of upper abdominal pain. The characteristic symptoms include attacks of painful abdominal spasm—which are precipitated not only by the intake of food but also by changes in posture—a premature feeling of fullness during meals (*blocage alimentaire précoce*), eructations, and even vomiting. The attacks are fre-

quently accompanied by palpitation and perspiration, and the disease may run a protracted course, but there is no such periodicity of symptoms as in peptic ulcer. Emaciation is a late sequel, and massive haematemesis may be an occasional complication.

The most common sites of the lesion are the lesser curvature, the antrum, and the posterior wall of the stomach; in one type of the disorder the whole of the stomach is involved (concretio ventriculi). But the primary lesion may also be situated outside the stomach. The author describes 4 cases of his own seen at the Cantonal Hospital, Chur, Switzerland, in which the primary lesion, bronchiectasis or pneumonia, was in the pleural cavity. Treatment, apart from that of the pulmonary condition and the gastritis, consists in giving frequent small meals, application of poultices, and administration of spasmolytics. In France, splanchnic nerve block and radiotherapy have been tried, with success in some cases. *R. Schneider*

396. **Extract of Pregnant Mares' Urine—Therapy in Chronic Duodenal Ulcer. (Five-Year Clinical Evaluation)**
Z. T. BERCOVITZ. *Gastroenterology* [*Gastroenterology*] **26**, 230–238, Feb., 1954. 6 refs.

At New York University–Bellevue Medical Center 30 patients suffering from duodenal ulcer were treated with an " anti-ulcer factor " (uroanthelone, " kutrol ") derived from pregnant mare's urine. The natural history of the ulcers had been determined in the majority of cases by observation while the patients received treatment with a placebo for periods up to 11 months. Basic treatment consisting in administration of protein hydrolysate in a syrupy mixture, and sedation with diphenhydramine was given in all cases.

Only 4 out of the 35 control patients improved, whereas 16 out of the 30 given kutrol were benefited, some to the extent of either being symptom free or having remissions of longer duration than before treatment. Complications of ulcer, such as perforation, requiring surgical intervention were not prevented however, and 8 of the 14 patients not benefited later required operation. [No full clinical, radiological, or therapeutic details are given.] *K. Gurling*

397. **Post-bulbar Duodenal Ulcer with Particular Reference to its Hemorrhagic Tendency**
J. M. SWARTS and M. L. RICE. *Gastroenterology* [*Gastroenterology*] **26**, 251–259, Feb., 1954. 6 figs., 19 refs.

In a recent 5-month period the authors have seen at the Veterans Administration Hospital, Memphis, Tennessee, 11 patients with a peptic ulcer distal to the duodenal cap, and in this paper a total of 18 cases of such post-bulbar ulcer are discussed. They consider that ulcers in this situation are not uncommon, although they could find only 112 similar cases specifically mentioned in the literature; the average incidence in several large series reported was 9·6% of all duodenal ulcers.

Severe gastrointestinal haemorrhage occurred in 13 of their 18 cases, and a high incidence of bleeding was also noted in previously reported series. Symptoms did not differ materially from those produced by duodenal ulcers in the usual site, but *x*-ray confirmation of post-bulbar ulceration was obtained in all cases examined radiologically. In 4 there was an associated deformity of the duodenal cap.

The authors state that post-bulbar duodenal ulcers have a greater tendency to bleed than those in the cap, that surgery is more often required in these cases, and that gastric resection is liable to be more difficult. *K. Gurling*

398. **The Use of Banthine in the Control of Gastric Acidity**
M. ATKINSON. *Gastroenterology* [*Gastroenterology*] **26**, 288–298, Feb., 1954. 3 figs., 13 refs.

The effect of " banthine " (methantheline) on gastric secretion was studied at University College Hospital, London, in patients with radiologically confirmed duodenal ulcer but without pyloric stenosis. In 10 fasting patients a single intramuscular injection of 50 mg. of methantheline reduced the acidity of the gastric secretion, the *p*H in 5 cases rising to at least 3·5 and exceeding 3 for an average period of 115 minutes starting 30 to 60 minutes after the injection; in the other 5 cases the *p*H rose to between 2 and 3. The volume of secretion which could be aspirated was reduced in all 10 cases. Injections of methantheline were given every 4 hours during the night, starting at 10 p.m., to 8 patients who had fasted for 4 hours before the first injection. Hourly sampling of the gastric contents showed that the *p*H remained below 2 in 4 patients, rose to between 2 and 2·8 for 3 hours in 2 others, and rose to over 3·5 6 hours after the first injection in the remaining 2. The volume of the residue at 9 a.m. (the last injection being at 6 a.m.) was reduced in only 3 patients. These unsatisfactory results were attributed to the retention of previously secreted acid, gastric emptying being delayed by methantheline. When these 8 and 2 other patients were given a similar series of injections together with a single dose of 8 g. of a powder containing equal parts of magnesium trisilicate, magnesium oxide, and calcium carbonate at 10.30 p.m., the *p*H of the contents exceeded 3 in 7 subjects from 10.30 p.m. to 6 a.m.

In 5 patients the effect of oral methantheline was studied. These patients were given a gastric diet and 4 doses of 8 g. of the alkaline powder during the 24 hours. Hourly samples of the gastric contents were aspirated for 24 hours and then, starting with a dose of 50 mg., methantheline was given 4 times a day by mouth half an hour before the alkaline powder, the dose being increased until side-effects were prominent. Methantheline given in this way had little effect on the daytime acidity in any of the patients, but did reduce the nocturnal acidity in 3 patients. It did not significantly reduce the pain of which 2 patients were complaining.

In 12 patients given a single injection of 50 mg., methantheline caused dryness of the mouth, and 8 of them also had blurred vision. In 11 of these patients the pulse rate was increased by 10 to 60 beats a minute, remaining above normal for at least 4 hours in 6 of them. Of 5 patients given 150 to 200 mg. every 6 hours by mouth, 3 had some difficulty in micturition.

In discussing his results and those of others, the author stresses the fact that observations on the secretion obtained by continuous gastric suction cannot be compared with those on secretion obtained, as here, by sampling techniques, which take into account the possible effects of drugs on motility and gastric emptying. Judged by its ability to increase the *p*H to at least 3 and to maintain it there, methantheline is here shown to be inadequate as an antisecretory drug, although it was effective in prolonging the action of alkaline powder.

Derek R. Wood

399. **Ambulatory Treatment of Duodenal Ulcers. Effects of Fruit Juice, Olive Oil, Hexamethonium, and Methantheline**

P. H. FRIEDLANDER. *Lancet* [*Lancet*] **1**, 386–390, Feb. 20, 1954. 21 refs.

The results of a clinical trial of blackcurrant juice, olive oil, hexamethonium bromide, and methantheline in the treatment of patients with duodenal ulcer are reported in this paper from the Central Middlesex Hospital, London. Each of 4 groups of 24 to 26 patients received one of these remedies over a period of 15 months, while a comparable control group received a syrup free from vitamin C. Progress was assessed clinically and radiologically at intervals of 3, 9, and 15 months from the start of treatment, the criteria being presence or absence of an ulcer crater (in all the cases there was a demonstrable ulcer crater at the beginning of the trial), changes in weight, amount of pain, and frequency of absence from work on account of symptoms.

There was no evidence that these remedies had any effect on symptoms or on the rate of healing, except that patients receiving methantheline experienced rather more rapid relief of pain than the others. Of 100 patients completing the trial (13 failed to attend and 12 developed complications necessitating a change of treatment), 61 still had an ulcer crater on *x*-ray examination and 33 had severe pain. There was no difference in the clinical course of the disease between patients under 40 years and those over 40. No constant correlation was found between radiological healing and the incidence of symptoms; of 12 patients in whom the ulcer appeared to have healed completely, 4 had had pain within the last month. On the other hand, several patients who still had an ulcer crater, as demonstrated radiologically, had been free from pain for 12 months.

[This paper, which will form a useful yardstick for judging other remedies, shows that it is practicable to use simple clinical criteria to assess the progress of even such a variable condition as duodenal ulcer.]

T. D. Kellock

400. **Value of Strict Dieting, Drugs, and "Robaden" in Peptic Ulceration**

P. R. C. EVANS. *British Medical Journal* [*Brit. med. J.*] 1, 612–616, March 13, 1954. 25 refs.

The author reports the results of a therapeutic trial involving 114 patients, 27 with gastric and 87 with duodenal ulcer, which he carried out at the Wrexham (Denbighshire) Group of Hospitals. [Unfortunately only a small proportion of these patients appear to have been followed up until radiological healing had taken place, although some information about the remainder was obtained in response to a questionary.] The patients were divided at random into four groups. All were treated by rest in bed for most of the day; Group 1 received strict diet alone, Group 2 strict diet plus "robaden" (a proprietary extract of intestinal mucosa), Group 3 a "post-ulcer diet" plus robaden, and Group 4 a post-ulcer diet alone.

Two conclusions are reached from the study of this small series. First, that the administration of robaden, given by the prescribed method, did not affect the rate of healing or of relapse of peptic ulcers. Second, that in patients on a post-ulcer diet the ulcers healed as well as in those on a strict diet.

[The small number of patients actually attending for follow-up examination (21 out of 114) throws doubt on the validity of these conclusions, but the absence of any evidence of more rapid healing of the ulcers in patients given any of the particular forms of treatment than in those treated only by rest in bed and the hospital regimen is notable.]

John Naish

401. **Potentially Reversible Renal Failure following Excessive Calcium and Alkali Intake in Peptic Ulcer Therapy**

F. X. DUFAULT and G. J. TOBIAS. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 231–236, Feb., 1954. 23 refs.

402. **Result of Vagotomy in Treatment of Anastomotic Ulcer**

B. W. WELLS. *Lancet* [*Lancet*] **1**, 598–599, March 20, 1954.

In order to assess the results of vagotomy in the treatment of anastomotic ulcer, the author followed up 39 cases, selected from the records of 8 London hospitals, which had been treated by vagotomy alone not less than 2 years previously. [It is stated in the text that cases might also be accepted for analysis less than 2 years after vagotomy if recurrence had already taken place. This would weight the figures against vagotomy. Reference to the tables, however, suggests that none were in fact accepted.] The ulcer followed gastro-enterostomy in 14 cases and partial gastrectomy in 25 (performed for duodenal ulcer in 23 and for gastric ulcer in 2). Strict criteria were applied to ensure that a positive diagnosis of anastomotic ulcer had been made in every case.

Of the 25 patients who had undergone partial gastrectomy, 15 had had no evidence of recurrence of ulceration; of the 10 in whom recurrence was proven or suspected, symptoms had returned within a year in 7. Of the 14 patients who had undergone gastro-enterostomy, only in 4 was there no evidence of recurrence, and again the symptoms had returned most commonly within a year of vagotomy.

The conclusion is drawn that although vagotomy is only partly satisfactory in the treatment of anastomotic ulceration after partial gastrectomy, it is safer than the alternative of a more radical gastrectomy and is worthy

of trial, whereas it has no place as the sole method of treatment for ulceration following gastro-enterostomy.

[This is a valuable report, although the paper is brief and there is no mention of the early results. The exclusive use of the term " recurrence " in the assessment of results suggests that all the ulcers healed initially after vagotomy, but it is more likely that many persisted.]

C. J. Longland

LIVER

403. **Uptake of Ammonia by the Brain in Hepatic Coma**
S. P. BESSMAN, J. F. FAZEKAS, and A. N. BESSMAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 66–67, Jan., 1954. 4 refs.

The authors found on measuring the ammonia content of arterial and venous blood in 3 cases of liver failure that there was evidence of increased ammonia uptake by the brain. They suggest that this might be due to the reductive amination of ketoglutaric acid to form glutamate, the removal of ketoglutarate from the Krebs cycle preventing regeneration of oxalacetate and further oxidative metabolism, this being a possible factor in the production of hepatic coma, in which a marked diminution of cerebral oxygen uptake has been observed by the authors.

G. S. Crockett

404. **Cation-exchange Therapy in Ascites due to Cirrhosis of the Liver.** (Kationenaustauschertherapie des Ascites bei Lebercirrhose)
W. FIEBIG. *Klinische Wochenschrift* [*Klin. Wschr.*] **32**, 193–196, March 1, 1954. 4 figs., 6 refs.

The author reports his experience with the use of cation-exchange resins in the treatment of 12 cases of ascites due to cirrhosis of the liver seen at the Moabit Municipal Hospital, Berlin.

Four cases of portal hypertension had shown no improvement following treatment with a low-salt diet (less than 2 g. of sodium chloride daily), mercurial diuretics, and drugs of the digitalis group. When 60 g. of the ammonium salt of the exchange resin was given daily, losses of from 7·2 to 13 kg. in body weight in 2 to 4 weeks were noted. A low-salt, high-protein diet was persisted with, but the simultaneous administration of mercurial diuretics was considered to be contra-indicated in view of the considerable acidosis which was produced by the treatment. This was partially corrected by the administration of sodium bicarbonate. For a further period [length not stated] reaccumulation of the ascites was prevented by a maintenance dose of 20 to 40 g. of the resin daily, plus a restricted salt diet. The liver function tests, however, remained abnormal throughout.

The other 8 patients were cases of true cirrhosis with varying degrees of liver failure. In 2 of them treatment with the ammonium salt of the resin had to be stopped because of toxic manifestations—drowsiness, confusion, and personality changes—which, however, cleared up on cessation of the treatment. Another 2 patients were given the hydrogen form of the resin with good effect on the ascites and without producing side-effects. The fall in the alkali reserve was no greater than with the ammonium salt. Finally, a resin was prepared which had the amino-acid methionine as its cation. A daily dose of 60 g. of this preparation produced good initial reduction of the ascites, although this was not complete and was again accompanied by a serious fall in the alkali reserve, which was treated as before.

In his summing up the author stresses: (1) that the follow-up period was too short to allow of assessment of the real value of this type of therapy; (2) that other measures, especially a low-sodium diet, must be taken at the same time; and (3) that complete clearance of the ascites was not achieved. All three forms of the resin contained 33% of potassium in order to prevent body depletion of this ion as a result of the loss of large quantities of ascitic fluid.

H. H. Reichenfeld

405. **Portal Cirrhosis: Correlation between the Severity of Esophageal Varices and Variations in Physical Findings**
E. D. PALMER and I. B. BRICK. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 149–151, Feb., 1954. 3 refs.

406. **Clinical and Biochemical Observations on the Use of Large Doses of Testosterone Propionate in Acute and Chronic Liver Disease**
F. M. MORGAN, G. K. WHARTON, P. STARR, and R. R. COMMONS. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **21**, 89–120, Feb., 1954. 15 figs., 30 refs.

Believing that the anabolic properties of testosterone propionate may be of value in liver disease, the authors have tried the effect of this hormone in the treatment of 17 patients with acute hepatitis and 26 with cirrhosis at the County General Hospital, Los Angeles, California. The average total dose was 3·7 g. of testosterone propionate injected intramuscularly over a period of 12 days. In 15 out of the 17 cases of acute hepatitis there was an improvement in appetite and well-being within 72 hours, and an increase in libido. The response in the cases of portal cirrhosis was less good, but all 5 cases of subacute alcoholic cirrhosis were greatly improved. Among the adverse effects it was noted that 5 of the 8 female patients developed hirsutism and other patients voice changes and acne, while in those with portal cirrhosis fluid retention became worse. Patients with acute hepatitis converted testosterone into urinary 17-ketosteroids more readily than did those with cirrhosis. Full details of biochemical investigations are given.

[All patients were given a high-protein diet with vitamin supplements, and sodium intake was restricted. It might therefore have been more instructive if the results of testosterone therapy in those with cirrhosis had been compared with a control period on this regimen alone. In acute hepatitis, improvement on admission to hospital is so usual that it is difficult to attribute it solely to coincident therapy.]

P. C. Reynell

See also Pathology, Abstract 297.

Cardiovascular System

407. **Tumor Metastasis to the Heart**
J. M. YOUNG and I. R. GOLDMAN. *Circulation* [*Circulation (N.Y.)*] **9**, 220–229, Feb., 1954. 5 figs., 40 refs.

A large series of tumor deaths was studied for cardiac metastases in a Veterans Administration Hospital [Memphis, Tennessee]. The incidence of cardiac metastasis in this somewhat selected group was 19·1%. The bulk of the cases were bronchogenic carcinoma, malignant melanoma, malignant lymphoma, and carcinoma of the pancreas and esophagus. Correlation of electrocardiographic changes and anatomic findings is given. Likewise, the behavior of the individual types of tumors with reference to pathologic findings is presented.—[Authors' summary.]

408. **Antibiotic Therapy of Bacterial Endocarditis. V. Therapeutic Considerations of Erythromycin**
J. E. GERACI and W. J. MARTIN. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **29**, 109–118, Feb. 24, 1954. 16 refs.

Experience in the treatment of bacterial endocarditis with erythromycin, although limited, has been disappointing. The authors have treated 7 such cases with this drug at the Mayo Clinic, the dosage being 0·3 to 0·5 g. 6-hourly; no drug toxicity was observed. In only one case, due to *Streptococcus salivarius*, was a good response obtained. Three patients died of toxaemia within 9 days, 7 days, and 36 hours respectively, and a fourth of cerebral embolism after 2 months. In all these cases the causative organism was *Staphylococcus aureus* and post-mortem examination revealed acute endocarditis. In the sixth case a good initial response was obtained but resistance emerged rapidly, while in the seventh no improvement was observed. These last 2 patients finally recovered after treatment with penicillin and dihydrostreptomycin. In these 2 cases the organisms responsible were respectively an enterococcus and *Streptococcus mitis*.

Sensitivity studies of the organisms were carried out in each case. There is evidence to suggest that erythromycin and bacitracin in combination may be more effective than either drug alone. The authors conclude that erythromycin should rarely be used in the treatment of bacterial endocarditis, and only in combination with bacitracin or streptomycin. *F. Starer*

409. **Lone Auricular Fibrillation**
W. EVANS and P. SWANN. *British Heart Journal* [*Brit. Heart J.*] **16**, 189–194, April, 1954. 4 figs., 7 refs.

Occasional cases of auricular fibrillation occur in which, even after the most careful investigation, especially to exclude thyrotoxicosis, the aetiology remains obscure. This condition is called " lone auricular fibrillation " by the authors, who here analyse a series of 20 cases seen at the London Hospital. All the patients were males, their ages ranging from 38 to 72, and the authors emphasize that the diagnosis of lone auricular fibrillation should rarely be made in women, in whom paroxysmal auricular fibrillation—a different condition—is more common. A relatively slow heart rate is characteristic, and there is no evidence of cardiac enlargement even when the condition has been present for 10 to 20 years, as in 6 cases in the present series. Similarly, electrocardiography reveals no ventricular preponderance, and cardiac failure never occurs. Embolism was not encountered among these patients. The prognosis is excellent and treatment rarely necessary. Quinidine should on no account be used. Occasionally a patient engaged in heavy work complains of palpitations, in which case 1 grain (65 mg.) of digitalis leaf may be prescribed daily in order to allay these symptoms.
A. Paton

410. **Studies of Pulmonary Hypertension. IV. Pulmonary Circulatory Dynamics in Patients with Mitral Stenosis at Rest**
P. N. G. YU, J. H. SIMPSON, F. W. LOVEJOY, H. A. JOOS, and R. E. NYE. *American Heart Journal* [*Amer. Heart J.*] **47**, 330–342, March, 1954. 2 figs., 37 refs.

In 43 patients with mitral stenosis the pulmonary arterial and pulmonary " capillary " pressures were found to be elevated in rough proportion to the degree of disablement. Where the resting mean pulmonary arterial pressure exceeded 30 mm. Hg, the calculated mitral valve area was 1 sq. cm. or less. It was concluded that determination of pulmonary " capillary " pressure is of value in eliminating chronic pulmonary disease as a factor in pulmonary hypertension; there was a general correlation ($r = 0{\cdot}825$) between pulmonary " capillary " pressure and pulmonary diastolic pressure at lower levels, but with extreme pulmonary hypertension this relationship was no longer valid. *J. McMichael*

411. **Studies on the Effect of Exercise on Cardiovascular Function. II. The Blood Pressure and Pulse Rate**
R. S. FRASER and C. B. CHAPMAN. *Circulation* [*Circulation (N.Y.)*] **9**, 193–198, Feb., 1954. 3 figs., 11 refs

The authors discuss the difficulties (and the conflicting results which have been reported) of measuring the changes in blood pressure which take place immediately after the cessation of exercise. At the University of Minnesota, the blood pressure of 11 young women (aged 22 to 30), 19 young men (18 to 39), and 11 older men (40 to 57) with no history of cardiovascular disease was recorded before, during, and after exercise on a treadmill, by means of a needle inserted into the brachial artery.

In each group there was a rise in systolic pressure and a fall in diastolic during exercise, the mean pressure changing little from the resting value. Immediately

after exercise, however, the systolic pressure fell abruptly in the men, while in the women the fall was more gradual. About 20 seconds after the end of the exercise there was a secondary rise in all three pressures (systolic, diastolic, and mean) in the older men, but in the younger groups a gradual rise in the systolic and mean pressures occurred. All pressures in the 3 groups of subjects had returned to their resting level, or very near to it, in 6 minutes, although the pulse rate was still raised by about 15%. Considerable variations from these average results were found in individual subjects.

The findings described are interpreted as being the consequence of a fall in peripheral resistance accompanied by a rise in cardiac output. *C. W. C. Bain*

DIAGNOSTIC METHODS

412. **The Genesis and Importance of the Electrocardiogram in Coarctation of the Aorta**
R. F. ZIEGLER. *Circulation* [*Circulation* (*N.Y.*)] **9**, 371–380, March, 1954. 9 figs., 8 refs.

The author carried out electrocardiographic studies at the Henry Ford Hospital, Detroit, on 57 patients, whose ages ranged from 10 days to 36 years, with coarctation of the aorta. The coarctation was uncomplicated in 38 cases, and was associated with patency of the ductus arteriosus in 8, intracardiac anomalies in 9, and anomalies of the aortic arch in 4.

Of the patients with uncomplicated coarctation, 12 were under 18 months of age; in these the electrocardiogram (ECG) showed signs of ventricular hypertrophy or right bundle-branch block most commonly; evidence of left ventricular hypertrophy was present in 3 cases, and of left bundle-branch block in 2; all those whose ECG initially showed right ventricular hypertrophy later developed right bundle-branch block, with or without left ventricular hypertrophy. All these patients survived infancy and underwent successful resection of the coarctation. Of the 26 patients over 3 years of age in this group, 8 had a normal ECG, while 11 had signs of right bundle-branch block and 7 of left ventricular hypertrophy.

Of the 8 cases of associated patency of the ductus arteriosus, electrocardiographic evidence of right ventricular hypertrophy was present in 2 (one in which the ductus was proximal to the coarctation, and one in which it was distal), of right ventricular hypertrophy (progressing to right bundle-branch block) in one, and of lone right bundle-branch block in one. In both of the patients with right bundle-branch block the ductus was inserted proximal to the coarctation. Left ventricular hypertrophy was present in another of these 8 cases, and the ECG was indeterminate in the remaining 3. Of the 11 patients with other complicating defects, 4 had electrocardiographic signs of left ventricular hypertrophy, 4 of right ventricular hypertrophy, and 2 of right bundle-branch block. In contrast to the patients with uncomplicated coarctation the mortality during early infancy was 60% in this group. In the whole series left ventricular hypertrophy was seen more frequently in adults, older children, or in infants with complicating lesions than in infants with uncomplicated coarctation of the aorta.

The author concludes that the presence of right ventricular hypertrophy at birth is the result of insertion of the ductus arteriosus proximal to the site of coarctation. In such cases right heart failure may even be present at birth, but regresses provided that the ductus closes normally, and the prognosis is usually good. On the other hand the presence of left ventricular hypertrophy at birth (often associated with progressive left ventricular failure which may prove fatal in infancy) is probably due to insertion of the ductus distal to the coarctation, the foetal descending aorta thus being normally supplied and there being no stimulus for the development of a collateral circulation, so that closure of the ductus after birth will throw a heavy strain on the left ventricle. The most common electrocardiographic pattern in infants with coarctation of the aorta is right bundle-branch block, either as a stage in the regression of right ventricular hypertrophy in cases with a proximal closed ductus, or in combination with left or right ventricular hypertrophy in cases with a patent ductus. The prognosis is much better in the former circumstance than in the latter.

J. F. Goodwin

413. **Studies Utilizing the Portable Electromagnetic Ballistocardiograph. V. The Importance of the Light Exercise Test in Clinical Ballistocardiography**
H. MANDELBAUM and R. A. MANDELBAUM. *Circulation* [*Circulation* (*N.Y.*)] **9**, 388–399, March, 1954. 8 figs., 25 refs.

In experiments carried out at the Jewish and Beth-El Hospitals, Brooklyn, New York, ballistocardiograms were recorded before and after light exercise from 400 normal subjects, 400 patients with angina pectoris, 225 patients who had recovered from myocardial infarction, and 400 patients with hypertension. In the normal group the ballistocardiogram after effort showed, in the majority of cases, an increase in amplitude of the H and JK complexes without alteration in the wave form; this was regarded as the normal ballistocardiographic response to exercise. Abnormalities were very infrequent under the age of 40 (one in 75 patients), but increased in frequency with advancing years.

In the group with angina 38 patients had an abnormal resting ballistocardiogram and 73% of the remaining 362 developed abnormalities after exercise. Of the patients with healed myocardial infarction, the majority showed no change or some deterioration in the ballistocardiogram after effort, but 55 patients showed some improvement. These patients were asymptomatic, and the improvement in the ballistocardiogram was considered to be a good prognostic sign. Of the 400 patients with hypertension, normal patterns were the rule in those under the age of 25 years, but abnormalities were found in patients with hypertension of long duration. The earliest change seen was a deepening of the K wave, associated with a sharpening of the IJ stroke or absence of the I wave; these changes were induced by exercise in 15 cases. Of 144 of these patients under the age of 50, 59 showed an improvement in the pattern after exercise. The presence

of fused H and J waves, often associated with tall H and L waves, was considered to indicate impaired myocardial function and was noted in 62 of the patients with hypertension.

The physiological basis of the ballistocardiographic changes after exercise is discussed, and the authors conclude that ballistocardiography after light effort is a test of great value in the assessment of cardiovascular disease.

J. F. Goodwin

414. **The Ballistocardiogram in Acute Rheumatic Fever**
W. B. ABRAMS and G. L. CHESLEY. *Circulation* [*Circulation (N.Y.)*] **9**, 400–407, March, 1954. 2 figs., 20 refs.

Ballistocardiograms were recorded at a U.S. Army hospital from 18 young adult males suffering from acute rheumatic fever, 13 of whom had clinical evidence of carditis. Of the 33 ballistocardiograms recorded from these 13 patients, 31 were normal, one showed slight abnormalities, and one was considered dubious because of low voltage. Of 12 ballistocardiograms from 5 subjects without overt cardiac involvement, 11 were normal and one showed slight abnormalities. Records obtained when the activity of the disease was subsiding were normal in all but 2 cases. Case histories and ballistocardiographic tracings are presented.

The authors conclude that the ballistocardiogram is normal in most mild cases of rheumatic fever, even when there is clinical and electrocardiographic evidence of active carditis.

J. F. Goodwin

CONGENITAL HEART DISEASE

415. **Total Pulmonary Venous Drainage through a Persistent Left Superior Vena Cava**
W. WHITAKER. *British Heart Journal* [*Brit. Heart J.*] **16**, 177–188, April, 1954. 12 figs., 8 refs.

With increasing use of angiocardiography and cardiac catheterization it is becoming apparent that persistence of the left superior vena cava is not an uncommon congenital abnormality. The 6 cases reported in the present paper were originally diagnosed on routine clinical and radiological examination, 5 having since been subjected to angiocardiography and cardiac catheterization to confirm the diagnosis. All the pulmonary veins drain into the persistent left superior vena cava, which joins the left innominate vein or right superior vena cava; thus fully saturated blood mixes in the right atrium with unsaturated blood from the systemic circulation. The left ventricle is supplied with blood which enters the small left atrium through an atrial septal defect. Systemic blood flow and blood pressure are usually low, whereas pulmonary blood flow is increased and there is often pulmonary hypertension. The condition is compatible with survival at least to the third decade, but dyspnoea, recurrent pulmonary infections, and failure to grow are usual. Right ventricular enlargement is present and the cardiac shadow on radiography has a characteristic "cottage-loaf" appearance owing to the enlarged ventricle below and the venae cavae above. Angiocardiography and cardiac catheterization will provide confirmatory evidence, but are not necessary for diagnosis. Operative treatment is both unnecessary and dangerous.

A. Paton

416. **Technique, Indications, and Results of Retrograde Valvotomy by the Arterial Route in Stenosis of the Pulmonary Orifice.** (Technique, indications et résultats de la valvulotomie rétrograde par voie artérielle dans la sténose pulmonaire orificielle)
C. DUBOST and C. D'ALLAINES. *Journal de chirurgie* [*J. Chir. (Paris)*] **70**, 105–121, Feb., 1954. 7 figs., 9 refs.

The authors describe a new technique of pulmonary valvotomy developed at the Hôpital Broussais, Paris, in which a retrograde approach is made to the valve via the left pulmonary artery. In their opinion valvotomy is indicated in cases of pure pulmonary valvular stenosis and of the trilogy of Fallot, and in those rare cases (about 7%) of the tetralogy of Fallot in which the stenosis is valvular and not infundibular.

The original transventricular technique of Brock suffers from the disadvantage that there is significant loss of blood during the repeated passage of instruments, while there is a risk of tearing the hypertrophied and fragile muscle of the ventricular wall (one fatal case is cited) and also the possibility of late aneurysm formation at the site of cardiotomy (as occurred 17 months after operation in a case described here). Moreover, repeated instrumentation with large, rigid sounds may cause cardiac irregularities and make control of haemorrhage difficult, which in turn may so increase the anxieties of the surgeon that he will be content with a less complete valvotomy than is desirable. With the retrograde method, on the other hand, the authors have been struck by the simplicity of the approach, the safety of the manipulations, and the remarkable tolerance of the heart to these manœuvres.

A left antero-lateral thoracotomy is performed through the 4th space with division of the 3rd and 4th costal cartilages, this incision permitting the surgeon to carry out the more rapid transventricular operation should the patient's condition require it. The pericardium is opened, the heart examined, and the left pulmonary artery and its branches to the upper lobe are mobilized and controlled—the main stem with a fine rubber catheter and the branches with thread. The highest and most posterior branch is dissected well into the hilum, where it is ligated and divided, and the proximal end is held open by stay sutures of silk, the main vessel and branches being occluded by traction on the ligatures. A fine, graduated, olive-tipped probe is passed into the open end of the divided artery, past the rubber tube controlling the main trunk, and engaged in the valvular orifice, the size and position (central or eccentric) of which are noted. The probe is then removed and a special valvulotome with double expandable blades is introduced in the same way. This instrument is rigid and curved to follow the pulmonary artery, and the degree of opening of its blades is regulated by means of a graduated screw. When the tip of the instrument has passed through the orifice the blades are opened a width of 7 to 8 mm. and withdrawn. This manœuvre is

repeated 3 times, the blades being progressively opened up to a maximum of about 23 mm., each fresh incision being made in the same plane. If necessary the valvotomy can be followed by passage of an expandable 3-bladed dilator. The divided branch of the pulmonary artery is then tied and the pericardium sutured loosely.

The technique is admittedly open to criticism on the grounds that it is more time-consuming than Brock's operation and that the approach to the valve from its convex side may make it difficult to find the orifice, with consequent danger that a false passage may be made. The authors consider, however, that their approach is safer for the patient, is better borne by the heart, and causes less anxiety to the surgeon than the Brock technique.

Among 25 cases in which this technique has been used there have been 4 deaths, one during the operation from ventricular fibrillation, the others in the first 48 hours after operation. (It was in one of these fatal cases that the aneurysm from a previous transventricular operation was found, as mentioned above.) The late results are stated to be comparable with those achieved by Brock and other surgeons using the transventricular method.

A. M. Macarthur

417. **The Surgical Treatment of Coarctation of the Aorta in Infancy.** (Traitement chirurgical de la sténose isthmique de l'aorte chez le nourrisson)
J. MATHEY, J. C. SOURNIA, J. P. BINET, O. SCHWEISGUTH, J. LABESSE, and J. NOUAILLE. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir.* (*Paris*)] **80**, 89–99, 1954. 4 figs., 6 refs.

The authors have studied 15 cases of coarctation of the aorta seen at the Hôpital des Enfants Malades, Paris, in children under the age of 2 years. Two types of coarctation are usually recognized: (1) the infantile, with a patent ductus arteriosus, a long hypoplastic segment, and an absence of collateral circulation which makes these cases unsuitable for operation; and (2) the adult type, with a short diaphragmatic stenosis, a closed ductus, and extensive collaterals. In 10 of the 15 cases in which anatomical studies were possible there was a short area of stenosis suitable for resection and well-formed collaterals, but the aorta above the stenosis was hypoplastic and in 2 cases the ductus was patent. The stenosis lay at the level of the ligamentum arteriosum or ductus, the origin of the left subclavian artery being a variable distance above it. Below the stricture the aorta was dilated.

Diagnosis is usually easy. The symptoms are dyspnoea and sometimes heart failure, the heart is enlarged by hypertrophy of the left ventricle, arterial pulsation in the upper limbs is energetic and the blood pressure raised, whereas in the lower limbs pulsation is feeble or absent. Rib notching is not seen in the chest radiograph, but this does not imply the absence of collateral circulation. The prognosis is bad, its gravity depending on the degree of left ventricular hypertrophy, but even when this is not marked, sudden death may occur or heart failure supervene rapidly. In the authors' series operation was not at first advised and 8 out of 10 patients died within 1½ to 18 months. As a result of operation on the remaining 5 children, 4 of whom were under the age of 12 months, 3 recovered immediately, and the fourth after a second operation for evacuation of a haemothorax; the fifth patient died of cardiac arrest. These 5 cases are described in detail. The operation was not difficult as there were no arteriosclerotic changes, and resection and end-to-end anastomosis with everting sutures was performed in each case. Pulsation in the legs and polyuria were observed after operation.

The authors conclude that operation is indicated in infants when enlargement of the left ventricle is marked and increasing; it is contraindicated if failure has occurred or if there is pulmonary congestion, as the risk is then prohibitive. If enlargement is moderate and stable it is best postponed until later in childhood.

M. Meredith Brown

CHRONIC VALVULAR DISEASE

418. **Surgical Treatment of Mitral Stenosis**
E. C. ANDRUS, A. BLALOCK, and W. R. MILNOR. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **67**, 790–802, Dec., 1953. 4 figs., 11 refs.

This paper is based on observations made on 75 patients with mitral stenosis, ranging in age from 20 to 49 years and comprising 17 men and 58 women, before and after surgical treatment at Johns Hopkins Hospital, Baltimore. The survivors have been followed up for periods ranging from 6 months to more than 3 years. Considerable (and sometimes dramatic) improvement resulted from the operation in nearly three-quarters of the cases, and has persisted in most of those followed up for 3 years. The indications for surgery are discussed, and it is stated that the results of valvotomy are usually better when the pulmonary arterial pressure is low in relation to the pulmonary capillary pressure, and are almost uniformly poor when the pulmonary vascular resistance has become fixed at a high level. Definite evidence of pulmonary congestion without marked (radiological) enlargement of the left auricle is a favourable sign. Cases with coincident aortic disease need careful assessment, since the relief of mitral stenosis in the presence of a tight aortic stenosis may precipitate mitral regurgitation. Where there is intractable right heart failure the results of operation are poor and the mortality prohibitive, while other contraindications are the presence of active acute rheumatism (as evidenced by a raised erythrocyte sedimentation rate) or of mitral incompetence as the dominant mitral lesion.

The operative results in this series are described as excellent in 34 cases, good in 17, and fair in 13; failure is reported in 2 cases where valvotomy could not be carried out for technical reasons, and there were 9 deaths (12%), 4 due to embolism, 4 to progressive cardiac failure, and one to staphylococcal pericarditis. It is noted that subjective improvement is often greater than can be measured by tests of pulmonary circulation and lung function.

The two most serious complications are embolism at operation and reactivation of rheumatic disease. The former is most likely to occur in the presence of auricular

fibrillation or of densely calcified valve cusps; temporary occlusion of the carotid arteries is recommended in order to reduce the risk of embolism while the finger is being introduced into the auricle or, in the case of a calcified valve, when the commissures are fractured. Active rheumatic heart disease recurred in 5 of the authors' cases despite the fact that penicillin was given during the immediate postoperative period, and in at least 5 others respiratory infection led to a worsening of symptoms after a favourable early response to operation; in one case there is evidence of recurrent stenosis. The need is emphasized for prophylaxis with sulphadiazine or penicillin against streptococcal infections of the respiratory tract to reduce the risk of reactivation of the rheumatic process after valvotomy.

Aschoff nodes are frequently found in the portion of auricular appendix removed at operation (40 times in 66 cases), but this finding is no guide to the likelihood of reactivation.

The authors conclude that " the need for surgical relief of mitral stenosis is determined by rheumatic fever. The ultimate success of this procedure will likewise depend on the subsequent control of that disease ".

(In the discussion following the presentation of this paper, Glover briefly reported a series of 500 cases, with satisfactory results in 76%, poor results in 10 to 15%, an operative mortality of 5·9%, and later death in 5%. Embolism occurred in 2·5% of these cases.)

F. J. Sambrook Gowar

419. **The Technical Problem of Mitral Commissurotomy. Results Obtained by Instrumental Dilatation of the Stenosis.** (Le problème technique de la commissurotomie mitrale. Résultats obtenus par la dilatation instrumentale de la sténose)

C. Dubost, G. Oteifa, and P. Blondeau. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir. (Paris)*] **80**, 321–329, March 10, 1954. 7 figs.

In this paper from the Hôpital Broussais, Paris, the normal and morbid anatomy of the mitral valve is reviewed, the authors pointing out that successful commissurotomy depends upon the state of the valve and of the left auricle, through which the approach is made. Three types of case are distinguished. In the first type there is simple fusion of the cusps at the commissures and digital dilatation is easy. In the second type access is difficult owing to the presence of organized clot in the auricle or appendage or to the narrowing of the mitral orifice in the form of a fibro-elastic ring which resists dilatation by the finger; cases of this type are suitably treated by instrumental section or dilatation. The third type consists of cases in which there is no access owing to an obliterated auricle and of cases with fixed stenosed valves, with the stenosis involving the papillary muscles and tendons and often complicated by gross mitral regurgitation; in this type valvotomy is impracticable. The case incidence of each type is of the order of 50%, 35%, and 10% respectively.

The authors have found valvulotomes unsatisfactory and prefer to use a spreading dilator (which is illustrated) similar to Brock's dilator for pulmonary stenosis. With this instrument the commissures can be split when digital dilatation fails, and fortunately splitting always occurs in the right place, no untoward damage having been caused in any of their cases. Of the last 40 cases of a large series, 4 underwent exploration only, 10 were treated by digital valvotomy, and in 26 instrumental dilatation was required. The 4 deaths which occurred were in the last-named group. *S. F. Stephenson*

420. **Respiratory Function in Mitral Disease in Relation to the Operation of Commissurotomy.** (La funzionalità respiratoria nella malattia mitralica in rapporto all'intervento di commissurotomia)

G. F. Della Penna and M. Gentile. *Archivio di chirurgia del torace* [*Arch. Chir. Torace*] **11**, 187–201, April–June, 1954. 1 fig., 20 refs.

Pulmonary function tests in patients with mitral stenosis reveal abnormalities which can be correlated with the pathological changes in the pulmonary circulation. Thus in 30 cases of mitral stenosis studied at the Institute of Surgical Pathology, Rome, the most important changes were a marked increase in minute ventilation and diminished vital capacity and maximum breathing capacity. These reflect the inelasticity of the lungs caused by the pulmonary congestion. On the other hand oxygen consumption at rest was relatively normal, so that the ventilation equivalent (minute ventilation divided by oxygen consumption) was increased, while the coefficient of oxygen utilization (oxygen consumption divided by minute ventilation) was decreased. On exercise there was some increase in oxygen consumption but an even greater increase in minute ventilation, so that the ventilation equivalent rose while the coefficient of oxygen utilization fell still further.

This is the exact opposite of the response to exercise seen in the normal subject, and can be interpreted in the patient with mitral stenosis as an increase in pulmonary ventilation without a comparable increase in blood flow through the lungs. Studies carried out in patients after recovery from mitral valvotomy showed an increase in pulmonary function of 15 to 35%. After exercise, oxygen consumption and minute ventilation increased proportionately, so that there was increased efficiency in removal of oxygen by the pulmonary circulation.

A. Paton

421. **The Pulmonary Capillary Pressure Curve in Relation to the Clinical Findings in 17 Cases of Verified Mitral Regurgitation.** (La courbe " capillaire pulmonaire " et les données cliniques dans 17 observations de régurgitation mitrale vérifiée)

P. Soulié, F. Joly, J. Carlotti, and J. R. Sicot. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **47**, 1–26, Jan., 1954. 6 figs., 17 refs.

In 17 cases of mitral stenosis with regurgitation, verified at operation, the results of cardiac catheterization and the clinical, radiological, and electrocardiographic findings were investigated in order to determine their value in assessing the presence and degree of mitral regurgitation. In 7 of the cases the volume of regurgitating blood was small and in 10 moderate. The pulmonary capillary tracings recorded from normal

subjects, patients with pure mitral stenosis, and those with associated regurgitation are discussed and compared. The following features in the tracing are stated to suggest regurgitation: (1) only the second of the two waves is well defined, whereas the first is far less distinct than in the normal tracing—in some cases it may be absent altogether or visible only as a deformation on the ascending limb of the second wave; (2) the high amplitude of the second wave indicates momentary hypertension, reaching 50 to 60 mm. Hg; this is attributed to the summation of a right ventricular pressure wave transmitted by the pulmonary artery plus a left ventricular pressure wave transmitted by the pulmonary veins through the incompetent mitral orifice.

In 250 of the authors' patients with mitral valvular disease tracings suggestive of regurgitation were found in 15, and of the 7 of these who were operated on, mitral regurgitation was found in 6. Among 120 patients who underwent commissurotomy, regurgitation was found in 17. In 7 of these cases the volume of regurgitating blood was small and in none of them was the capillary pressure tracing abnormal; in the remaining 10 cases the reflux was moderate, and in 6 out of 8 of these cases in which the capillary pressure was recorded it was suggestive of regurgitation. No radiological sign was found to be of any diagnostic value.

The authors conclude that no one single sign can be regarded as wholly reliable in the diagnosis of mitral regurgitation. The three most reliable signs, which should be considered together, are: (1) an apical systolic murmur; (2) the electrocardiogram taken in conjunction with catheterization (the former may show evidence of left ventricular strain, combined left and right ventricular strain, or present a normal record in the presence of a pulmonary arterial pressure over 45 mm. Hg); (3) the pulmonary capillary pressure tracing. Small degrees of regurgitation cannot be recognized by any method. Any aggravation of mitral reflux by operation seems to manifest itself only in changes in the pressure readings, there being no apparent adverse clinical effects.

A. Schott

422. **Rheumatic Manifestations Provoked by Commissurotomy.** (Les évolutions rhumatismales provoquées par la commissurotomie)

P. Soulié, Y. Bouvrain, P. Fortin, J. di Matteo, and R. Tricot. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **47**, 49–59, Jan., 1954.

Among 100 patients subjected to mitral commissurotomy, reactivation of acute rheumatism by the operation was thought likely or possible in 10 cases, and in this paper these are discussed in some detail. It is pointed out that in order for a diagnosis of reactivation to be made, a sufficiently long interval of freedom from rheumatic symptoms before the operation must have elapsed, and that the diagnosis of acute rheumatic fever must be established with reasonable certainty, despite the absence of any specific diagnostic tests.

In 4 of the present cases it appeared that reactivation could reasonably be assumed as in 3 of them no evidence of any rheumatic activity had been present for 6, 13, and 30 years respectively, and in the fourth case the patient had never had acute rheumatic fever at any time. In these 4 cases the interval between operation and recrudescence ranged from 24 hours to 2 months. In another 2 cases the operation was performed too soon after a previous attack of rheumatic fever for the infection to be considered inactive at the time of operation, and in a further 2 the recurrence took place too long after the operation to be attributable to it. In the remaining 2 cases the rheumatic nature of the postoperative condition was doubtful. No relation was found between the degree of mitral stenosis, the condition of the valve, or the degree of surgical trauma and the likelihood of reactivation of acute rheumatism.

[Some relevant papers on the histological findings in biopsy specimens of the left auricle are discussed, but unfortunately without any bibliographical references; those interested in this aspect may wish to consult the following: Enticknap, *Brit. Heart J.*, 1953, **15**, 37; Decker *et al.*, *Circulation* (*N.Y.*), 1953, **8**, 161 (*Abstracts of World Medicine*, 1954, **15**, 101).] *A. Schott*

423. **Recent Experience of Mitral Commissurotomy in 230 Cases.** (230 cas de commissurotomie mitrale. Acquisitions nouvelles)

F. d'Allaines, C. Dubost, and P. Blondeau. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir.* (*Paris*)] **80**, 314–321, March 10, 1954. 3 refs.

Between February, 1951, and February, 1954, the authors performed mitral valvotomy at the Hôpital Broussais, Paris, in 230 cases, with an operative mortality of 8·7% (20 deaths, including 4 during operation). Of this total, 105 cases have been reviewed more than 6 months after operation, when 85 showed good or excellent results, while in 20 they were assessed as moderate or poor. [The results in the first 100 of these cases have been previously reported at some length (*Mém. Acad. Chir.* (*Paris*), 1953, **79**, 572; *Abstracts of World Medicine*, 1954, **15**, 225).]

Omitting the obvious indications for valvotomy, the authors review the more equivocal factors in the light of their experience. In their opinion, advanced age alone is no bar to operation, nor is cardiac arrhythmia a contraindication, although its presence entails close examination of other adverse factors. In nearly half their cases showing auricular fibrillation the results were moderate or poor. Little correlation was found between the presence of auricular thrombi and the incidence of pre- and postoperative embolism. In 10% of their patients there was preoperative pyrexia, probably not due to active rheumatism. Although in these cases auricular thrombi are often present, their course and results have been normal.

Among 35 patients operated upon following right ventricular failure there were 5 deaths, and on examination at 6 months the result in 14 of the survivors was satisfactory and in 8 unsatisfactory. Severe right heart failure was treated on 4 occasions by inferior vena caval ligation and three times by high spinal analgesia, after which valvotomy was successfully carried out. Mitral regurgitation is only diagnosed with certainty at operation, and the authors analyse the very variable clinical findings in 47 of such cases in their series. Cardiac catheteriza-

tion was not of great value in diagnosing regurgitation, and exploration is advised in doubtful cases. Prognosis is based mainly on the anatomical lesion found and the over-all impression at the end of operation.

S. F. Stephenson

CORONARY DISEASE AND MYOCARDIAL INFARCTION

424. **The Etiology of Cardiac Enlargement in Coronary Occlusion, Hypertension, and Coronary Artery Disease**
A. M. MASTER. *American Heart Journal* [*Amer. Heart J.*] **47**, 321–329, March, 1954. 40 refs.

Enlargement of the heart, in cases of coronary occlusion, has hitherto been generally attributed to hypertension. This opinion was based on erroneous definitions of hypertension, since the variations of pressure in different age groups and in the sexes were not taken into account. We have, therefore, reconsidered the causation of cardiac enlargement in such cases, using the newly established limits of hypertension.

Of the 500 men who suffered coronary occlusion, 136 had had hypertension, 332 had had normal pressure, and 32 were borderline cases. Seventy-seven of the 500 (15·4%) had definite enlarged hearts. Of these 77, 29 had hypertension, 45 had normal blood pressure, and 3 were borderline cases. The frequency of cardiac enlargement in those with hypertension was 21·3%, and in those with normal blood pressure it was 13·6%. At least 27 of the patients with normal pressure and large hearts had never been in heart failure. Heart failure, therefore, is not an essential factor in the production of cardiac enlargement in those with normal blood pressure. Hypertension does not predispose to ventricular aneurysm any more than does normal blood pressure. Cardiac enlargement was more frequent in the hypertensive patients in each age group. It seems clear, then, that hypertension is a factor in the causation of enlargement of the heart, in those who suffer from coronary occlusion. The incidence of enlargement of the heart increased sharply at the age of 55 in patients with normal blood pressure. Age, with its associated coronary sclerosis is also an important cause of cardiac enlargement in coronary occlusion. When both hypertension and coronary sclerosis (the aging process) occur simultaneously, the incidence of cardiac enlargement is most frequent—almost two-fifths of the cases of coronary occlusion.

Among the 100 women studied, 44 had enlargement of the heart. The ratio of cardiac enlargement among the women was almost three times that among the men—44·0% to 15·4%. This higher frequency was found among the hypertensive group—women 52·2% and men 21·3%, as well as among those with normal blood pressure—women 23·8% and men 13·6%. Hypertension occurred in 71% of the female patients and in 27% of the male patients. Since 71% of the women with coronary occlusion had hypertension, and since 44% had cardiac enlargement, hypertension appears to be an important cause of enlargement of the heart in women. In women with coronary occlusion the frequency of cardiac enlargement was greatest in the 60 to 64 year age group when coronary sclerosis and hypertension both occurred most often. Since 21% of the women had a normal blood pressure, and since 23·8% of these had an enlargement of the heart, coronary sclerosis alone also appears to be a cause of cardiac enlargement.

The combination of hypertension and coronary sclerosis (the aging process) is the most important factor in the causation of enlargement of the heart in patients who suffer from coronary occlusion.—[Author's summary.]

425. **Electrokymography in Ventricular Aneurysm following Cardiac Infarction**
P. AMUNDSEN. *Journal of the Oslo City Hospitals* [*J. Oslo City Hosp.*] **4**, 17–25, Feb., 1954. 5 figs., 4 refs.

The principle of electrokymography is the registration by means of a sensitive photo-electric cell of the movements of the cardiac contour in the form of a curve which is recorded synchronously with an electrocardiographic tracing. From an analysis of the electrokymograms recorded at Ullevål Hospital, Oslo, in 2 cases of aneurysm of the left ventricle due to cardiac infarction, in which the records obtained from the aortic arch, the apex of the left ventricle, the base of the left ventricle, and the aneurysmal area were correlated, the author suggests that the electrokymogram is of value in the diagnosis of cardiac aneurysm. The characteristics of the electrokymogram in these 2 cases were: (1) during the ejection phase of ventricular systole the electrokymogram showed either no, or very little, movement of the aneurysmal contour, whereas the normal ventricular wall showed a marked inward movement; (2) during the following diastolic phase the aneurysmal contour showed an inward movement while the ventricular wall was shown to move outwards. *William A. R. Thompson*

426. **The Effect of Estrogens on the Plasma Lipids in Coronary Artery Disease**
M. F. OLIVER and G. S. BOYD. *American Heart Journal* [*Amer. Heart J.*] **47**, 348–359, March, 1954. 6 figs., 31 refs.

427. **Perforation of the Infarcted Inter-ventricular Septum**
J. C. SCHLAPPI and D. G. LANDALE. *American Heart Journal* [*Amer. Heart J.*] **47**, 432–436, March, 1954. 1 fig., 12 refs.

Since 1845 a total of 93 cases of perforation of the infarcted interventricular septum have been reported in the literature, all but 17 of them in the last 20 years. In this paper from the County General Hospital, San Diego, California, the authors describe 3 further cases, in each of which there was electrocardiographic evidence of simultaneous infarction of the anterior and posterior walls; in all cases the murmurs and thrill of a septal defect developed from one to 3 days later. Two of the patients, a man aged 63 and a woman aged 68, died from right ventricular failure within a fortnight; the third patient, a woman aged 73, was living 6½ years later although with signs of chronic right ventricular insufficiency. *C. W. C. Bain*

428. **Studies on the Effect of Exercise on Cardiovascular Function. III. Cardiovascular Response to Exercise in Patients with Healed Myocardial Infarction**
C. B. CHAPMAN and R. S. FRASER. *Circulation* [*Circulation (N.Y.)*] **9**, 347–351, March, 1954. 1 fig., 5 refs.

The response of the cardiovascular system to moderate physical exertion in 9 patients who had had a myocardial infarction at least 6 months previously was studied and compared with that in 12 healthy subjects of the same age group. The cardiac output, circulation time, and blood pressure, which were determined before, during, and after 10 minutes' exercise on a motor-driven treadmill, showed very similar changes in both groups. The pulse rate, however, rose by 56% in the patients compared with 37% in the controls. This excessive acceleration of the pulse was probably related to physical inactivity rather than to cardiac disability. In view of these findings it is suggested that restriction of physical activity is not called for in the routine management of symptomless patients with healed myocardial infarction.

J. McMichael

429. **Hemodynamic Studies of Patients with Myocardial Infarction**
W. W. SMITH, N. S. WIKLER, and A. C. FOX. *Circulation* [*Circulation (N.Y.)*] **9**, 352–362, March, 1954. 9 figs., 13 refs.

Cardiovascular function was studied at Bellevue Hospital, New York, in 10 normal subjects, 10 patients with arteriosclerosis, 10 patients with acute myocardial infarction without shock, 9 patients with acute myocardial infarction with shock, and 12 patients who had recovered from myocardial infarction 6 weeks to 13 months previously. The cardiac output, estimated by the Hamilton dye method, was found to be about half the normal value in the patients with shock due to myocardial infarction; in those without shock the average value was higher, though individual values overlapped. With recovery, the values obtained in both groups approached, but did not quite reach, the normal average value. Variations in peripheral resistance were found to play as great a part in the production of a fall in blood pressure in myocardial infarction as variations in cardiac output. The average cardiac output of the arteriosclerotic patients (age 62 to 77) was lower than that of the normal subjects (age 21 to 55). *J. McMichael*

430. **The Long-term Prognosis following Myocardial Infarction, and Some Factors which Affect It**
D. R. COLE, E. B. SINGIAN, and L. N. KATZ. *Circulation* [*Circulation (N.Y.)*] **9**, 321–334, March, 1954. 23 refs.

The long-term prognosis after the first attack of myocardial infarction was studied from the records of 285 patients at Michael Reese Hospital, Chicago, who had the initial attack between 1932 and 1942 and survived the first two months. (It is stated that the immediate mortality during the first two months was 23%.) Of the 285 patients, 191 lived over 5 years, 125 over 10 years, and 29 over 15 years. The long-term prognosis was rather better in younger patients, females as well as males. Associated hypertension and diabetes had no effect on immediate mortality, but adversely affected the long-term survival. Angina, which was present in 60% of the cases before the first attack of infarction, improved the chance of long survival, especially if the duration was more than one year. The chance of survival, both immediately after the infarction and later, was diminished in patients with congestive failure and gallop rhythm. Shock affected the immediate prognosis but, unlike heart failure, had no effect on long-term survival. The authors state that the presence of pulmonary embolism during the first attack " practically excludes the possibility of prolonged survival ". In patients who were at rest at the time of onset of the infarction the prognosis was less favourable than in those who were exercising or were under emotional stress. Tobacco and alcohol appeared to have little influence on prognosis. Generally, the prognosis was better in patients with a low leucocyte count during the week following the initial attack.

On the whole the electrocardiogram (ECG) was not a satisfactory guide in prognosis, although the chance of long-term survival appeared to be favourable in patients with subendocardial-infarct patterns in the ECG and least good in those with septal and atypical patterns. The immediate prognosis was better in cases of infarction of the anterior wall than in cases of posterior-wall infarction, but the long-term prognosis was about the same in both. Arrhythmia and even the milder forms of heart block had an adverse effect on long-term survival.

The authors state that the best guide to prognosis after the initial attack is the patient's ability to resume active life. Of those patients who became fully active, 71% lived over 10 years. The most frequent cause of death was another attack of myocardial infarction, but the longer the patient survived after the initial attack, the better the chance of surviving a subsequent infarction.

T. Semple

HEART FAILURE

431. **Gitalin in the Treatment of Congestive Heart Failure: a Clinical Study**
A. WEISS and F. STEIGMANN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 188–192, Feb., 1954. 7 refs.

Interest has recently been revived in gitalin, a water-soluble mixture of glycosides first isolated by Kraft from *Digitalis purpurea* in 1912. In the clinical study here reported from Cook County Hospital, Chicago, it was used in 49 cases of congestive heart failure in order to determine its efficacy, dose required, toxicity, and ratio of the therapeutic to the toxic dose. The amount of drug required for initial digitalization was from 4·0 to 9·5 mg., the average being 5·9 mg., and the time taken to effect digitalization ranged from 1 to 5 days, averaging 2·6 days. Digitalization could be achieved in one day by giving the drug 6-hourly, 2 mg. for the first two doses and then 1 mg.

No toxic effects were noted in this part of the study, but in a further investigation the dose was increased in 4 cases until toxic effects were produced. This required rather more than twice the dose necessary to produce

digitalization. Maintenance studies were carried out in 20 cases and showed that the usual maintenance dose was 0·5 mg. Doubling this dose produced toxic effects in only 2 out of 9 patients, and when the dose was trebled a further 2 patients developed toxic symptoms after 10 to 12 weeks; the other 5 exhibited no evidence of toxic effects. The authors conclude that gitalin is an effective preparation with a wide margin of safety.

C. Bruce Perry

432. **Heart Failure in Chronic Pulmonary Disease.** [In English]
N. G. M. Orie, F. S. P. van Buchem, and B. P. A. A. Homan. *Acta medica Scandinavica* [*Acta med. scand.*] **148**, 123–134, March 12, 1954. 1 fig., 40 refs.

The factors concerned in the development of heart failure in chronic pulmonary disease, especially pulmonary arterial pressure, arterial oxygen saturation, and bronchial infection, were studied in 20 cases in which pneumonectomy had been performed, 10 cases of sarcoidosis, 13 of pure pulmonary stenosis, 20 of uncomplicated emphysema, and 6 of emphysema complicated by infection. As a result of their observations the authors conclude that right heart failure in these cases is produced by a combination of mechanical factors and infection, and that either of these acting alone rarely causes failure. They suggest that infection interferes with aeration, thus causing hypoxia, and they agree with other workers that when the arterial oxygen saturation falls below 80% heart failure is likely to occur.

Arthur Willcox

PERICARDIUM

433. **Acute Benign Pericarditis. I. Clinical Aspects. II. Electrocardiography.** (Pericarditis agudas benignas. I. Clínica. II. Electrocardiograma)
R. B. Podio, C. Baudino, J. Orgaz, I. Cresta, and J. Iudicello. *Revista argentina de cardiología* [*Rev. argent. Cardiol.*] **20**, 271–297, Sept.–Oct., 1953. 9 figs., bibliography.

A series of 21 cases of acute benign pericarditis were studied at the Italian Hospital, Córdoba, Argentina. No single aetiological agent was found, but 10 of the patients had recently had an upper respiratory tract infection and others had had pleural effusion, haemothorax, coronary thrombosis, and haemolytic anaemia (one case each). In 20 cases the initial symptom was pain of sudden or gradual onset, typically retrosternal and precordial and worse on respiration, compression, or movement. All patients had fever either before or with the pain (in contrast to myocardial infarction where fever follows pain). A friction rub developed in 15 cases, and there was unilateral or bilateral pleural involvement in 9 cases; cough and dyspnoea were marked only in these 9 cases. A pericardial effusion was detectable by percussion or radiography in 6 cases, in all of which the fluid was absorbed spontaneously. In most cases there was sinus tachycardia and moderate hypertension. The erythrocyte sedimentation rate was raised, generally to a greater extent than is usual after a coronary thrombosis. All the patients recovered in 1 to 10 weeks without any apparent sequelae; 10 patients who were treated with various antibiotics did no better than those treated symptomatically.

The electrocardiogram (ECG) was recorded with standard and with unipolar limb and chest leads and was examined for deviations in the S–T segment and changes in form and sign of the T wave. A detailed analysis of the findings is given, and the authors conclude that the ECG is of diagnostic value in 85% of cases. In addition to the characteristic signs of pericarditis (elevation of the S–T segment and inverted T wave), flat, diphasic, or notched T waves were often seen. There was little difference between the cases with an effusion and those without, except that a deep negative T wave was more common with effusion. The clinical course of the disease was not very closely reflected in the ECG, but it was considered that serial tracings are very helpful in assessing progress.

D. Goldman

434. **Acute Non-specific Pericarditis. Study in 24 Cases Including Descriptions of 2 with Later Development into Constrictive Pericarditis.** [In English]
H. Krook. *Acta medica Scandinavica* [*Acta med. scand.*] **148**, 201–218, March 23, 1954. 2 figs., 41 refs.

The author suggests that the incidence of acute non-specific pericarditis, a term used to describe those cases of pericarditis in which no systemic or local causal agent can be demonstrated, has increased in the last decade, and shows that it has become the commonest form of pericarditis seen at Malmö General Hospital, Sweden. In the 10-year period 1943–52, 64 cases of pericarditis occurred in patients over 15 years of age (excluding those cases seen in association with anaemia, myocardial infarction, and tumours of the heart), and of these, 21 were diagnosed as acute non-specific pericarditis, compared with 12 cases of rheumatic and 6 of tuberculous pericarditis, the two next largest groups. It was notable that the annual number of such cases had risen from 2 in 1943 to 8 in 1952—" an increase that can hardly be ascribed to chance ". Because of the clinical similarity between this disease and myocardial infarction the records of all cases of the latter condition occurring in subjects under 45 in the same period were scrutinized, and in 3 or perhaps 4 of these it was considered that the diagnosis should have been acute non-specific pericarditis.

The outstanding clinical feature of the disease in these 24 cases was the occurrence, during a mild upper respiratory tract infection in a young adult or middle-aged male, of a suddenly developing, severe, substernal or precordial pain, characteristically aggravated by cough and deep breathing. Fever appeared early, as did a loud, widespread pericardial friction rub. The symptoms generally subsided quite rapidly without residual cardiac damage, but there was a tendency for early, and sometimes repeated, recurrences to occur. The differential diagnosis from myocardial infarction depends upon the character of the pain, the time of onset, intensity and distribution of friction, the course of the temperature curve, and the electrocardiographic changes. Rheu-

matic, tuberculous, and purulent pericarditis are differentiated by their characteristic features. The author gives a detailed account of 2 cases diagnosed as acute non-specific pericarditis in which this condition was followed after 6 and 20 months respectively by constrictive pericarditis, confirmed at operation. He claims that this is the first time that such a sequence has been demonstrated. *Bernard Isaacs*

SYSTEMIC CIRCULATORY DISORDERS

435. **Comparison of Hypotensive Action of Sodium Azide in Normotensive and Hypertensive Patients**
M. M. BLACK, B. W. ZWEIFACH, and F. D. SPEER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 11–16, Jan., 1954. 3 figs., 9 refs.

Sodium azide, used experimentally as a cancer inhibitor, was found to have a hypotensive action which was more pronounced in patients with hypertension than in normal subjects. Given in doses of 0·6 to 1·3 mg. by mouth 3 to 4 times daily, sodium azide produced a sustained lowering of the blood pressure for as long as 2 years without ill effect—indeed its hypotensive action appeared to increase on repeated administration. The site of action of the drug is not known. *G. S. Crockett*

436. **Endocrine Treatment of Essential Hypertension.** [In English]
S. A. BORGSTRÖM. *Acta medica Scandinavica* [*Acta med. cand.*] Suppl. 290, 1–70, 1954. 34 refs.

In this paper from Stockholm the author describes the good results obtained with a combination of sex hormone and calcium therapy in long-standing cases of essential hypertension which had proved refractory to ordinary conservative treatment. By contrast, renal hypertension was relatively unresponsive. Treatment consisted in intramuscular injections of 6 mg. of diethylstilboestrol dimethyl ether, 10 mg. of testosterone propionate, and 5 ml. of calcium gluconate solution, given together every 2 weeks until there was an "adequate reduction" in blood pressure. For maintenance, tablets containing ethinyl oestradiol and methyl testosterone were given by mouth. All patients received adequate doses of vitamins A, B, C, and D in addition.

The author gives details of 51 personal cases. A further case has been described at length by the patient, a doctor (Ekehorn, *Acta med. scand.*, 1954, Suppl. 289). *K. G. Lowe*

437. **Results of Methonium Treatment of Hypertensive Patients, Based on 250 Cases Treated for Periods up to 3½ Years, Including 28 with Malignant Hypertension**
F. H. SMIRK. *British Medical Journal* [*Brit. med. J.*] **1**, 717–723, March 27, 1954. 3 figs., 18 refs.

The author summarizes his experience of the use of methonium derivatives in the treatment of 250 cases of hypertension seen at the University of Otago, Dunedin, over a period of 3½ years. Hexamethonium bromide was usually given by subcutaneous injection, but in some cases hexamethonium and pentapyrrolidinium were given by mouth. He compares the mortality figures in his treated cases with those in a comparable control series and in cases from the literature. Of one group of 28 patients with malignant hypertension, 21 survived for an average of 23 months; the mean survival time from the start of treatment in the remaining 7 was 9 months. Of 11 patients in the control group with malignant hypertension, 9 died. In patients with less severe hypertension the mortality was lower among those receiving hexamethonium (20 out of 122 patients) than among controls (15 out of 53 patients). In the treated patients headache and giddiness were relieved and there was marked improvement in cardiac and renal function and in retinal signs and symptoms. It is claimed that cardiac failure in hypertension can be effectively treated by methonium compounds without recourse to digitalis, mersalyl, and salt restriction, but it is emphasized that these results can be achieved only if rigorous attention is paid to the management of these cases.

[This is a very important contribution, which should be studied in the original for the very detailed findings.] *Bernard Isaacs*

438. **Hypertension Resulting from Unilateral Renal Vascular Disease and its Relief by Nephrectomy**
J. E. HOWARD, M. BERTHRONG, D. M. GOULD, and E. R. YENDT. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **94**, 51–85, Feb., 1954. 13 figs., 45 refs.

The clinical history is described in detail of 6 cases of severe, rapidly progressive hypertension due to unilateral kidney disease in which the hypertension was relieved by removal of the diseased kidney. In 2 of the cases appendicectomy was performed for unexplained episodes of right-sided abdominal pain, but the appendix in both cases was normal. Subsequently severe hypertension developed. No abnormality was seen on the intravenous pyelograms. Eventually the right kidney was removed, and microscopical examination of the tissue revealed an area of infarction with surrounding tubular atrophy; the cause of infarction was not known. Two further patients with mild, labile hypertension of some years' duration were admitted to hospital because of a sudden and severe deterioration in their condition. Intravenous pyelography showed a non-functioning kidney, although the retrograde pyelogram was normal. After nephrectomy both patients continued to have mild hypertension. Microscopical examination of the removed kidney showed uniform atrophy of the renal tubular epithelium in one case and foci of severe tubular atrophy in the other. At operation in these 2 cases the renal artery was found to be small and to pulsate poorly, but it could not be adequately explored for any evidence of obstruction. The fifth patient had an episode of right renal colic which was followed 4 months later by severe hypertension. Ureteric catheterization revealed a reduction in the flow and in the sodium concentration of the urine from the right kidney, but an intravenous pyelogram was normal. Arteriography disclosed an obstruction at the origin of the right renal artery. After nephrectomy the blood pressure became normal.

In the sixth case, that of a 4-year-old boy, the intravenous pyelogram was normal but on arteriography obstruction to the left renal artery was observed. At operation a ganglioneuroma was found attached to the left renal pedicle; after removal of the tumour and the left kidney the blood pressure returned to normal. In the last 2 cases, in which arteriography demonstrated the presence of renal ischaemia, the histological appearances were surprisingly normal, the only significant change being prominence of the juxtaglomerular bodies in one case and foci of slight parenchymal atrophy in the other.

K. G. Lowe

439. **Stages of Salt Exchange in Essential Hypertension**
D. M. GREEN, A. D. JOHNSON, W. C. BRIDGES, and J. H. LEHMANN. *Circulation* [*Circulation (N.Y.)*] **9**, 416–424, March, 1954. 6 figs., 17 refs.

At King County Hospital (University of Washington School of Medicine), Seattle, the excretion of sodium chloride by 26 normotensive and 53 hypertensive patients was studied under basal conditions, after intravenous sodium chloride loading, and during osmotic diuresis induced by the infusion of mannitol. It was found that the salt excretion of about 60% of the hypertensive patients was within the normal range, while the others excreted considerably more salt than normal in the various circumstances studied. The patients who excreted salt freely were those with a raised plasma filtration fraction and normal filtration of sodium; in the patients who excreted only normal amounts of salt the glomerular filtration rate was low. It is suggested that a high rate of salt excretion is to be found in patients with hypertension in an early stage, where filtration is maintained at a normal level in face of a reduction in renal plasma flow; later, the filtration rate falls off and salt excretion approximates to normal levels.

[Details of the cases studied are given only in tabular form and the duration of known hypertension in each is not stated; this makes it difficult to evaluate the claim that the " high-salt-excretors " were in an early stage of hypertension. The possibility that the patients studied were not all suffering from the same type of hypertension is not considered.] *D. A. K. Black*

440. **Arterial Piezography in Hypertension and Arterial Disorders.** (La piézographie artérielle. Son intérêt dans l'hypertension et les atteintes artérielles)
E. DONZELOT, A. MEYER-HEINE, and E. CHARTRAIN. *Presse médicale* [*Presse méd.*] **62**, 379–381, March 10, 1954. 17 figs., 7 refs.

The authors describe and discuss the value of carotid arterial pressure tracings recorded by means of Bartholi's piezograph with variable condenser and frequency modulation, the record (interrupted at intervals of one-fiftieth of a second) being obtained photographically from the screen of the cathode-ray oscillograph.

Tracings taken in cases of hypertension show characteristic and progressive changes in comparison with the normal piezogram; as hypertension increases, the ascending limb of the primary wave becomes prolonged and the plateau at or after the summit is modified or disappears; and as peripheral resistance increases, the dicrotic wave becomes less distinct from the primary wave.

Although some abnormality is always found in hypertension, there may be a surprising dissociation between the height of the blood pressure and the degree of change; there is, however, a striking correlation between the severity of the disease and the form of the curve, and the piezograms of patients with similar symptoms may be almost identical in spite of widely differing blood-pressure readings. A patient with high arterial tension but a normal piezogram can be assumed to have little arterial disease and a good prognosis, whereas a person with moderate hypertension but advanced piezographic changes must be regarded as having severe vascular disease.

In cases of atherosclerosis or arteriosclerosis the piezogram is almost always abnormal, even when the blood pressure is normal, and cases of latent arteriosclerosis may be brought to light by this method where there is a family history of arterial disease. On the other hand a normal tracing may be obtained in cases of cardiac infarction or angina pectoris in young subjects although follow-up will usually reveal the gradual development of abnormal features. The proportion of normal records obtained from persons in good health diminishes with age after the 50th year. *R. S. Stevens*

441. **Circulatory Changes in the Lower Limb following Lumbar Sympathectomy**
D. MESSENT and P. BEACONSFIELD. *Surgery* [*Surgery*] **35**, 382–389, March, 1954. 3 figs., 11 refs.

At the Postgraduate Medical School of London, changes in blood flow in the calf and foot resulting from lumbar sympathectomy were measured in 17 patients. Observations were made before, during, and after operation, frequent readings being taken during the immediate postoperative period from 7 calves and 6 feet, and at intervals up to 3 months from 13 calves. The series included cases of organic arterial disease.

The average results may be summarized as follows. Induction of anaesthesia increased the flow considerably above the resting values in both calf and foot, and a further small increase resulted immediately from the sympathetic neurectomy. One hour after operation the flow in both calf and foot had increased still more, though that in the foot on the untreated side had returned to normal. The calf flow then declined rapidly for several days, after which the rate of fall became slower; the preoperative level was not reached in the 3-month period of observation. The blood flow in the foot reached its peak some 4 hours after operation and then declined a little in the next 48 hours; it was not followed further. Thus the delay in development of maximum flow for 24 hours or more reported by others in the hand and foot was usually not seen in this series, and it is suggested that any such delay is more apparent than real and that the maximum dilator effect of sympathectomy is to be expected immediately after operation.

C. J. Longland

Haematology

442. **Some Immunohematologic Results of Large Transfusions of Group O Blood in Recipients of Other Blood Groups. A Study of Battle Casualties in Korea**
W. H. CROSBY and J. AKEROYD. *Blood* [*Blood*] **9**, 103–116, Feb., 1954. 12 refs.

The authors report a study carried out at the 46th U.S. Army Surgical Hospital in Korea during the winter of 1952–3 of the effect of transfusion of large quantities of Group-O whole blood—the so-called universal-donor blood—upon the erythrocytes of recipients whose blood groups were A, B, or AB. The plasma of the transfused blood, of which as much as 37 U.S. pints (16·8 litres) were given in one case, had been previously screened for the presence of abnormally high titres of anti-A and anti-B isoagglutinins, but not for immune forms or haemolysins.

In all, 25 cases were followed up, cell survival counts being made by the Ashby technique and the serum examined for passively acquired antibodies. The foreign anti-A and anti-B agglutinins were demonstrable (in the cold) in about half the cases, and most showed selective destruction of the recipient's cells. These two phenomena were not necessarily linked, and loss of the patient's erythrocytes sometimes occurred when no circulating foreign antibodies could be identified. This destruction, especially in patients of blood groups A and AB, is considered to be due to other forms of anti-A not demonstrable by usual laboratory methods, since no incomplete antibodies or haemolysins could be found.

No clinical signs characteristic of transfusion reactions were noted and no delay in recovery occurred, so that the procedure of screening the plasma seemed justified. For the period during which transfused anti-A and anti-B agglutinins were present group-specific blood could not be cross-matched and the continued use of Group-O blood was necessary during convalescence.

J. S. Campbell

443. **Treatment of Polycythaemia Vera with Radiophosphorus. Haematological Studies and Preliminary Clinical Assessment**
J. D. ABBATT, H. CHAPLIN, J. M. M. DARTE, and W. R. PITNEY. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **23**, 91–104, Jan., 1954. 3 figs., 19 refs.

In this paper from the Medical Research Council's Radiotherapeutic Research Unit and the Postgraduate Medical School of London encouraging results are reported in the treatment of 27 cases of polycythaemia vera with injections of radioactive phosphorus (^{32}P). In 22 cases there was full remission of all signs and symptoms lasting at least 6 months; in the remaining cases there was symptomatic response without full remission of signs. Preliminary venesection was not performed. Each patient received a single injection of 5 to 8 millicuries of ^{32}P as inorganic phosphate, a second injection being given if a satisfactory remission was not obtained. Patients were discharged from hospital on the third or fourth day after the injection, provided the 24-hour urinary excretion of ^{32}P was 100 millicuries or less.

Examination of the blood revealed a reduction in the number of platelets about 20 days after the injection. The authors believe that the drug exerts its effect upon a primitive stem-cell precursor of the cellular elements of the blood in the bone marrow. The platelet count was lowest 30 to 50 days after the injection. Eventually the average platelet count was 210,000 per c.mm., as compared with 640,000 per c.mm. before treatment. No similar correlation was observed between remission and the decrease in the number of leucocytes. Furthermore, there was a poor correlation between the increase in the haematocrit value and the increase in total blood volume.

Although marked symptomatic relief was often noted within a few days of the injection, the maximum response was not manifest for 3 to 4 months. From the sixth week there was regression in the size of the spleen, haemorrhagic and thrombotic tendencies disappeared, and such symptoms as pruritus cleared up.

A. Garland

ANAEMIA

444. **Specificity of Auto-antibodies in Acquired Haemolytic Anaemia**
J. V. DACIE and M. CUTBUSH. *Journal of Clinical Pathology* [*J. clin. Path.*] **7**, 18–21, Feb., 1954. 5 refs.

Until now it has generally been assumed that the auto-antibodies found in acquired haemolytic anaemia are non-specific and unrelated to those of any known blood group. But cases have recently occurred which seemed to refute this assumption, and in this paper from the Postgraduate Medical School of London the authors describe the results of a detailed investigation of the specificity of the antibodies present in 10 patients suffering from acquired haemolytic anaemia. In all cases the direct Coombs test was positive, and cold antibodies were present in very low titre only. Serum from these patients was tested against known erythrocytes, both by the trypsin technique and by the use of antiglobulin serum. Wherever possible, eluates were prepared from the erythrocytes and tested for the presence of antibodies. The results in 3 cases are described in some detail.

Some of the patients were found to have both a specific antibody and a " warm " non-specific antibody, and some of these specific antibodies were against antigens which the patient did not possess and were therefore considered to be immune antibodies (all 10 patients had previously received blood transfusions). But in half the cases the antibody (" auto-antibody ") was active against an antigen present in the patient's own erythrocytes. In the 5 cases in which patients formed an auto-antibody reacting with specific antigens the antibody was found to

have specificity within the Rh system—one patient had anti-e plus anti-C, another had anti-e plus anti-D, and 3 patients had anti-e antibodies. It was remarkable that although anti-D is formed so readily as an immune iso-antibody, only one of the 9 patients who were D-positive formed anti-D as an auto-antibody. In contrast, anti-e, which is so seldom found as an immune iso-antibody, was formed by 5 patients as an auto-antibody. In most cases auto-antibodies without apparent specificity were also present. *R. F. Jennison*

445. **The Sickle Cell Trait in Jamaica**
D. B. JELLIFFE, K. L. STUART, and V. G. WILLS. *Blood* [*Blood*] **9**, 144–152, Feb., 1954. 1 fig., bibliography.

The average Jamaican is of African descent with a varying degree of Caucasian admixture, but there are also Indian and Chinese communities amongst the population. Blood smears were examined from 2,116 members of different racial groups, mostly school-children, and provided no evidence of the sickle-cell trait among Chinese and Caucasians, while a single positive finding among the Indian group seemed to be due to inapparent African ancestry; among three groups of predominantly African descent, however, sickling was found in 5·7, 3·9, and 3·6% respectively. The authors discuss the geographical distribution of the sickle-cell trait, and suggest that it may have originated in India and from there found its way to Africa and thence to Jamaica.

[It should perhaps be pointed out that the statement made here that the abstracter and Cutbush (*Brit. med. J.*, 1952, **1**, 404; *Abstracts of World Medicine*, 1952, **12**, 135) have suggested that the sickle-cell trait was spread to Africa by the migration of the Veddoids of India to East Africa by sea is incorrect. The most likely explanation for the occurrence of the trait in both Africa and India is a common inheritance from the Veddoids of Arabia.] *H. Lehmann*

446. **Isolation of Castle's Intrinsic Factor. (Preliminary Communication)**
A. L. LATNER, R. J. MERRILLS, and L. C. D. P. RAINE. *Lancet* [*Lancet*] **1**, 497–498, March 6, 1954. 10 refs.

Further to their previous work (Latner *et al.*, *Brit. med. J.*, 1953, **1**, 467; *Abstracts of World Medicine*, 1953, **14**, 224) the authors, working at Durham University, now believe they have succeeded in isolating Castle's intrinsic factor from a crude extract of human gastric juice without the use of electrophoresis. The major part of the intrinsic factor can be extracted by use of a suitable buffer solution at *p*H 6·35, while the active fraction finally obtained is easily soluble at *p*H 2·0.

This fraction showed a close similarity to the active fractions obtained, as previously described, by electrophoresis of concentrates of human gastric juice and hog pyloric mucosa. Both methods have yielded material which is highly effective in diminishing the faecal excretion of radioactive vitamin B_{12} administered orally. These various fractions (which, as judged by their electrophoretic characteristics, appear to be homogeneous) are mucoprotein in nature. The behaviour in the ultracentrifuge of this active material isolated without the use of electrophoresis indicates that it contains a small amount of protein of high molecular weight which sediments rapidly, and that the remaining 95% is homogeneous, with a molecular weight less than 20,000, probably of the order of 15,000. *D. G. Adamson*

447. **Oral Treatment of Pernicious Anaemia with Intrinsic Factor Concentrate and Vitamin B_{12}**
C. P. LOWTHER, W. D. ALEXANDER, and E. B. HENDRY. *Lancet* [*Lancet*] **1**, 495–497, March 6, 1954. 9 refs.

The authors report, from the Western Infirmary, Glasgow, good results from the oral treatment with intrinsic factor and vitamin B_{12} (cyanocobalamin) of 20 patients (8 men and 12 women) suffering from pernicious anaemia who had previously been maintained in complete remission by injections of liver extract or vitamin B_{12}. The preparation used, "bifacton", was in tablet form and each tablet contained 1·5 g. of extract of hog pyloric mucosa and 7·5 μg. of vitamin B_{12}. Half the patients were given 2 tablets and the other half 4 tablets daily. No signs of haematological or neurological relapse were seen after 6 months' treatment.

[As the authors point out, however, 6 months is too short a time in which to evaluate fully the effect of a haematinic in pernicious anaemia. It is known that in some cases of pernicious anaemia in full remission relapse following cessation of treatment may occur after a much longer period.] *D. G. Adamson*

448. **The Haematinic Action of Penicillin in Megaloblastic Anaemia and its Relationship to B_{12} Metabolism and the Intestinal Flora**
H. FOY and A. KONDI. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **48**, 17–41, Jan., 1954. 3 figs., bibliography.

From the results of the treatment of 24 selected cases of severe megaloblastic anaemia in Africans in Kenya with penicillin, vitamin B_{12}, and folic acid, separately and in combination, the authors conclude that there are at least three well-defined types of megaloblastic anaemia among Africans: (1) those that respond to the oral or intramuscular administration of penicillin or to the oral administration of vitamin B_{12} (cyanocobalamin); (2) those that will not respond as in Group 1, but respond to intramuscular vitamin B_{12}, crude liver, or folic acid; and (3) those that respond only to crude liver or folic acid. It is possible to distinguish the groups only by their response to treatment; clinically and haematologically there is no difference, the megaloblasts in the bone marrow being usually typical, although some are of the intermediate (or transitional) form—but these are not necessarily associated with a higher erythrocyte count. In this paper full reports are given of the 16 cases belonging to Group 1. [Reports of representative cases of all three types, drawn from the same series, are given in a previous paper by the same authors (*Lancet*, 1953, **2**, 1280), which otherwise covers much the same ground and for that reason is not abstracted here. Readers interested in the subject should, however, study both papers in the original.—EDITOR.]

The patients were not malnourished; some had intestinal parasites, but their presence or absence was not correlated in any predictable way with the type of anaemia; only one had vitamin deficiency (a pellagrin). The usual dose of penicillin was 200,000 units orally or 400,000 units intramuscularly each day for 7 to 17 days. The reticulocyte response to this dosage was maximal, starting within 5 to 10 days, and the haemoglobin value and erythrocyte count doubled within 14 to 21 days, the bone marrow reverting to normoblastic activity. Of the 8 patients who did not respond to oral penicillin, 4 were in Group 2—all these had achlorhydria—and 4 were in Group 3—none of these had achlorhydria.

Discussing possible explanations, the authors express the opinion that the penicillin-responsive megaloblastic anaemia results from habitual use of a high-carbohydrate, low-protein diet, which produces an intestinal environment inimical to the synthesis and utilization of vitamin B_{12}, and that the administration of penicillin changes the ecological equilibrium of the intestinal flora and alters the balance between bacteria synthesizing vitamin B_{12} and those competing for it. Since the site of synthesis of vitamin B_{12}, so far as is known, is in the colon while the site of its absorption appears to be in the ileum or jejunum, they suggest that the diet favoured by these Africans permits bacteria, some of which are known to have a great avidity for vitamin B_{12}, to ascend in greater numbers than usual into the small intestine.

Megaloblastic nutritional anaemias associated with the use of a high-carbohydrate, low-protein diet occur in many other countries, and may be similar in aetiology to those occurring in Kenya. *M. C. G. Israëls*

NEOPLASTIC DISEASES

449. **Cutaneous Reactions in the Lymphoblastomas**
A. ROSTENBERG and S. M. BLUEFARB. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **69**, 195–205, Feb., 1954. 27 refs.

It is known that the lympho-reticular tissues are intimately connected with antibody production, and experimental investigations have shown that there is some disturbance of this function in cases of lymphoblastoma, in which those tissues are predominantly affected. The present authors have studied the persistence, in 56 patients with various forms of lymphoblastoma or leukaemia, of cutaneous reactions to antigens to which the patient had presumably been exposed before the onset of the disease. The antigens used were tuberculin, trichophytin, oidiomycin, histoplasmin, histamine (1 in 100,000), and a histamine-liberator, " Compound 48-80 ". Tuberculin tests were carried out with old tuberculin, and the patient was regarded as tuberculin negative only on failing to react to a concentration of 1 in 10. Immediate reactions were checked after 20 minutes, and delayed reactions after 72 hours or, in a few cases, 48 hours. A general depression of reactivity to the antigens was observed, this being more marked in respect of delayed reactions. The development of an immediate weal to histamine and to the histamine-liberator was, however, unimpaired. There was no difference in effect between diseases of the "lymphosarcoma" group (including Hodgkin's disease, lymphoblastoma, mycosis fungoides, reticulum-cell sarcoma, and chronic lymphatic leukaemia) and those of the " myelogenous " group (including acute leukaemia, myelogenous and monocytic leukaemia, and multiple myeloma). Nor was their any uniformity in the loss of delayed reactivity to the various antigens. *Kate Maunsell*

450. **Thrombocytopenia and Abnormal Bleeding in Multiple Myeloma**
T. N. JAMES, R. W. MONTO, and J. W. REBUCK. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 1281–1287, Dec., 1953. 3 figs., 19 refs.

At the Henry Ford Hospital, Detroit, the authors studied the pathogenesis of the haemorrhagic tendency observed in cases of multiple myelomatosis. In 58 proved cases of the disease the bone marrow was deficient in megakaryocytes. The platelet count, which was determined by the method of Rees-Ecker, was below 170,000 per c.mm. in 22 out of 31 cases. In the authors' experience haemorrhage is uncommon when the platelet count exceeds this figure. Although there are few reports of thrombocytopenia in association with multiple myelomatosis, the authors consider that the former was the chief cause of the haemorrhage in these cases. Other causes are discussed; in 2 cases cryoglobulinaemia was thought to be responsible.

The diagnosis of multiple myelomatosis was confirmed in all cases by the demonstration of myeloma cells in the bone marrow. *Nigel Compston*

451. **The Effect of Pyridoxine Deficiency Induced by Desoxypyridoxine on Acute Lymphatic Leukemia of Adults**
D. R. WEIR and W. A. MORNINGSTAR. *Blood* [*Blood*] **9**, 173–182, Feb., 1954. 6 figs., 6 refs.

Pyridoxine deficiency causes a decrease in the number of circulating lymphocytes in animals, and regression of lymphosarcoma has also been observed in rats after its induction. To induce pyridoxine deficiency in man a pyridoxine-deficient diet may be used, but this is most unpalatable. Alternatively, the condition can be induced without dietary restriction by means of a pyridoxine antagonist, desoxypyridoxine. Pyridoxine deficiency is indicated by the appearance of seborrhoeic dermatitis, and to achieve this between 500 and 1,000 mg. of desoxypyridoxine must be administered daily.

The authors report the results of such treatment in 4 cases of acute lymphatic leukaemia. In one case the administration of the drug was followed by a clinical and haematological remission, but a subsequent relapse did not respond to a further course of treatment. In the remaining cases there was no clinical improvement, although the administration of desoxypyridoxine was associated with a decrease in the number of circulating lymphoblasts. Necropsy revealed retention of normal architecture and reticulo-endothelial hyperplasia in the spleen and lymph nodes, possibly indicating a modification of the leukaemic process, in 2 of the 3 cases in which it was performed. *Nigel Compston*

Respiratory System

LUNGS AND BRONCHI

452. **Aerosols of Pancreatic Dornase in Bronchopulmonary Disease**
A. SALOMON, J. A. HERCHFUS, and M. S. SEGAL. *Annals of Allergy* [*Ann. Allergy*] **12**, 71–79, Jan.–Feb., 1954. 1 fig., 16 refs.

Aerosols of "pancreatic dornase" (desoxyribonuclease) were used by the authors at the Boston City Hospital (Tufts College Medical School) in the treatment of 35 patients, mostly with asthma or emphysema, of whom 17 had bouts of high temperature. A total dose of 150,000 to 600,000 units was given within a period of 2 to 6 days, 1 to 3 treatments being given daily. The authors noted that after each treatment cough became more effective, the sputum thinner and less viscid, and the 24-hour sputum output increased in volume 2 or 3 times. [No details of these volumes are given.] The authors emphasize that the results were best where much tenacious secretion was impeding respiration, and were less striking in those patients [the majority] who had chronic asthma or emphysema as an underlying condition, with an infection superimposed upon it. "A potent bronchodilator aerosol" was also given when bronchoconstriction was present.

[As about half the patients treated were suffering from an acute febrile condition with a rapidly changing clinical picture, it is difficult to accept the optimistic conclusions of the authors that the substance is a "useful aid in the evacuation of viscous, tenacious, mucopurulent secretions".] *H. Herxheimer*

453. **Hamman–Rich Syndrome. Analysis of Current Concepts and Report of Three Precipitous Deaths following Cortisone and Corticotropin (ACTH) Withdrawal**
J. W. PEABODY, H. A. BUECHNER, and A. E. ANDERSON. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 806–824, Dec., 1953. 7 figs., 31 refs.

The authors describe 3 cases which were regarded as examples of the acute diffuse interstitial fibrosis of the lungs described in 1944 by Hamman and Rich. The duration of symptoms from onset to death was 5½ months, 25 months, and 9 years respectively, and the histological changes, while resembling in every respect those described by Hamman and Rich only in the first case, seemed in the others to represent a more chronic phase of the same process, consistent with the longer duration of symptoms. In none of the cases was any evidence relevant to the aetiology obtained, either during life or post mortem, and no response to antibiotics was observed. Cortisone or ACTH (corticotrophin) was given in every case. In the first, which was in a relatively acute phase, there was remarkable radiological clearing of the lungs and symptomatic improvement during the administration of the hormones, but shortly after the gradual withdrawal of cortisone there was an acute exacerbation of dyspnoea and cyanosis with a return of the original *x*-ray appearances, and despite large doses of cortisone and ACTH the patient died within 24 hours of respiratory insufficiency. The second patient also died with severe respiratory difficulty shortly after the end of a 3-week course of cortisone which had produced no objective evidence of improvement. The third patient received moderate doses of ACTH for 27 days and became very breathless after reduction of the dosage. In spite of reinstitution of treatment with large doses of ACTH together with cortisone, he died of respiratory failure.
J. G. Scadding

454. **Loeffler's Syndrome, with a Report of Twenty Three Cases**
L. MARK. *Diseases of the Chest* [*Dis. Chest*] **25**, 128–149, Feb., 1954. 34 figs., 12 refs.

The author describes 23 cases diagnosed as of Loeffler's syndrome on the basis of abnormalities in the chest radiograph and eosinophilia in the blood. All the patients had respiratory symptoms and more than half complained of wheezing. Many were febrile and in about one-quarter the radiographic opacities were recurrent and migratory. Good results are claimed for treatment with blood transfusions and with cortisone. It is considered "necessary to include all transitory or disappearing shadows with eosinophilia as cases of Loeffler's syndrome".

[None of these cases appears to have resembled those described by Loeffler, and it is difficult to understand why they should be identified with the syndrome named after him. Pulmonary eosinophilia and its classification have been very fully discussed by Crofton *et al.* (*Thorax*, 1952, **7**, 1), whose paper is not mentioned by the author.]
J. R. Bignall

455. **Air-containing Cysts of the Lung**
J. R. BELCHER and A. H. M. SIDDONS. *Thorax* [*Thorax*] **9**, 38–45, March, 1954. 8 figs., 24 refs.

Of the many varieties of cyst of the lung which may contain air, there are five which bear some clinical relationship to each other, as follows: (1) bronchogenic, (2) post-infective, (3) infantile tension cysts, (4) anepithelial, and (5) emphysematous. The authors discuss these types on the basis of their surgical experience in a total of 76 cases.

The bronchogenic cyst is of developmental origin, and is seen microscopically to possess all structural layers. The postinfective cyst has fibrous walls, often with an epithelial covering; following a staphylococcal infection the wall is likely to be thin and the cavity to be distended as a result of a check-valve mechanism in the bronchus. The clinical features in 17 cases of the former and 8 of the latter were very similar, the presenting symptoms being those of bronchitis in 17, haemoptysis in 2, pneumo-

thorax in 1, and empyema in 2, 3 cases being disclosed on routine radiographic examination. The distinguishing radiological features are the presence of a cavity wall, although this may be filamentous in the staphylococcal type, of a fluid level, and of a surrounding pneumonitis. Surgical resection is advisable if there is evidence of recurrent infection or repeated spontaneous pneumothorax.

Three cases of infantile tension cyst are described, and it is suggested that they may be caused by abnormalities of the pulmonary veins or bronchial mucosa forming a check-valve mechanism. These infants usually present with severe dyspnoea and cyanosis, and radiographs of the chest show a huge pulmonary translucency causing marked mediastinal displacement. The treatment is by surgical resection, but preliminary decompression by drainage may be necessary.

The anepithelial cyst, of which 9 cases were seen by the authors, may be developmental in origin, and has a lining membrane consisting of layers of macrophages. It is connected to the hilum by a pedicle, and is trabeculated by condensed bronchial and vascular bundles.

The emphysematous cyst, on the other hand, is not pedunculated, and is commonly associated with local or generalized emphysematous changes; 39 cases are included in the authors' series. Both types of cyst give rise to dyspnoea either because of mechanical pressure or owing to development of a pneumothorax, while the emphysematous type may, in its advanced stages, be associated with cor pulmonale. Radiologically, both show as areas of increased translucency, with or without visible walls. In both types resection is advised if pulmonary function tests and radiographs suggest that dyspnoea is due to mechanical pressure and if advanced generalized emphysema is absent. Similarly, recurrent pneumothorax may call for surgical intervention.

J. N. Harris-Jones

456. **Electron Microscopic Observations of Pulmonary Alveoli**

R. H. SWIGART and D. J. KANE. *Anatomical Record* [*Anat. Rec.*] **118**, 57–63, Jan., 1954. 8 figs., 16 refs.

In an attempt to resolve the long-standing controversy as to whether or not there is a complete respiratory membrane separating the pulmonary alveoli from the capillaries the authors studied sections of the lungs of female white rats under the electron microscope at the University of Minnesota School of Medicine, Minneapolis. The animals were anaesthetized with ether and the lungs then perfused through the right ventricle with a buffered 1% solution of osmic acid. Tissue slices were excised, immersed for 8 hours in the same fixative, washed, dehydrated, and embedded in a prepolymerized medium by standard techniques. Sections 0·05μ thick were cut and mounted on nickel grids.

Every section examined showed some material intervening between the air space and the capillary which appeared to be a continuation of the alveolar septal stroma. This stroma did not resemble either the endothelial or the epithelial cytoplasm; it had the appearance of a reticulum containing endothelial cells and epithelioid cells, a small proportion of which were modified to form septal cells. There were occasional free macrophages in the alveoli, but these did not appear to be derived from the septal cells. Some sections showed intercellular fibrillar material between the endothelium and the alveolar spaces, but there was no evidence of the existence of a continuous epithelial lining between the smaller alveoli and the capillaries; nor was there any evidence of the existence of intervening non-nucleated plaques.

D. Goldman

457. **A Clinical, Radiographic, and Pathological Study of Pulmonary Embolism**

J. G. MACLEOD and I. W. B. GRANT. *Thorax* [*Thorax*] **9**, 71–83, March, 1954. 12 figs., 8 refs.

The authors, working at the Western and Eastern General Hospitals, Edinburgh, have studied 60 cases of pulmonary embolism in an attempt to correlate the pathological changes in the lungs with the clinical and radiographic manifestations. There were 12 deaths in the series.

The source of the embolus was a lower limb vein in 60% of cases; it was not identified in 11 cases, in most of which organic heart disease was present, with auricular fibrillation in 6 of them. Pleuritic pain occurred in 90% of cases and haemoptysis in 50%, the latter being more common in patients with pulmonary congestion secondary to heart disease. Signs suggesting a pleural effusion were present in several cases, but were usually found to be due to a high hemidiaphragm.

Opacities were present in the radiograph of the chest in 95% of cases and were of three types: pleural, intrapulmonary (resembling the opacity of pneumonic consolidation), and linear. The classic well-defined, triangular opacity was never seen. An elevated hemidiaphragm with inhibited movement or, occasionally, true paralysis was found in 50% of cases. The appearance of the opacities, particularly of the linear type, tended to change rapidly, and repeated radiographs at intervals of 4 or 5 days were found to be useful in diagnosis. The average time taken for resolution of opacities in cases with heart disease (48 days) was more than double that in cases without heart disease (23 days). Linear opacities, uncommon in the presence of heart disease, were found as frequently as pleural opacities and more frequently than intrapulmonary opacities in cases without heart disease.

Histological examination of the pathological material available showed that the infarcts were either "complete" (haemorrhagic), in which case prolonged ischaemia produced necrosis of the alveolar walls and dilated bronchial arteries caused an influx of blood, or "incomplete", in which case there was local congestion and oedema, but the anoxia was insufficient to produce necrosis. The former type was more commonly found in the presence of generalized pulmonary congestion, to which is attributed the slower resolution of opacities in such cases. In several cases an intrapulmonary opacity was shown at necropsy to have resulted from an infarct of much smaller size, and it is suggested that the shadow, which is often ill-defined, is largely caused by

local congestion and oedema bordering on an area of complete infarction. Linear opacities are presumed to represent local pleural reaction over the site of a pulmonary infarct which may itself not be visible.

E. G. Rees

458. **Pulmonary Fibrosis.** [In English]
O. J. BROCH, T. MOE, and M. WEHN. *Acta medica Scandinavica* [*Acta med. scand.*] **148**, 189–200, March 23, 1954. 45 refs.

After reviewing the literature on the pathogenesis of pulmonary fibrosis the authors describe 54 cases of this condition and 23 cases of Boeck's sarcoidosis affecting the lungs, seen at the Rikshospital, Oslo, in the period 1940–50. The diagnosis of fibrosis of the lungs was based on the radiological appearances. In only a few cases, apart from those due to sarcoidosis, was it possible to identify the causal disease. The onset of symptoms could be related to an acute respiratory illness in no more than one-sixth of the cases, and in 10 instances the fibrosis was discovered incidentally during radiological examination.

In describing the course of the disease the authors stress that once the fibrotic changes in the lungs have reached a maximum they tend to remain stationary, and that the progressive disability is then due to the development of secondary cardiovascular changes. At the time of the follow-up [presumably in 1953] all the patients with sarcoidosis were still alive, but 20 of those with fibrosis had died, 18 of them from cor pulmonale. At post-mortem examination carried out in 6 of these cases, "myomatosis" (honeycomb lung) was found in one case, while the remaining 5 showed only fibrosis, bronchiectasis, and some bronchopneumonic change.

[This report would have been more valuable if the diagnostic criteria of pulmonary fibrosis had been more clearly defined, and if it had been possible to correlate the clinical features with the pathological lesion.]

Bernard Isaacs

459. **Friedländer Pneumonia.** [In English]
R. KOLUMIES and H. LAITINEN. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **43**, 27–38, 1954, 3 figs., 23 refs.

In this paper from the University Medical Clinic, Helsinki, the authors discuss the incidence and features of pneumonia due to Friedländer's bacillus. A survey of the records of bacteriological cultures of the sputum in 1,041 cases of infection of the respiratory tract, made at the State Serum Institute and the University in the period 1931–51, showed that the organism first described by Friedländer in 1882 (now named *Klebsiella pneumoniae*) was present in 28 cases. In only 9 of these, however, were there also clinical and radiological signs of active pneumonia, the organism being present in 6 cases probably as a secondary invader, and in 3 cases as the primary cause.

The earliest clinical features of typical Friedländer pneumonia are those suggestive of bronchopneumonia in the upper part of one lung. Radiologically, the lungs may show small, round areas of consolidation, sharply circumscribed, and producing a dense shadow. Later, the foci coalesce, giving the appearance of a pseudolobar pneumonia, with the formation of abscesses, accompanied during recovery by fibrosis of the lung. Some of these cases develop very slowly, with equally slow recovery. The abscesses may break down to form cavities which may be confused with those of tuberculosis.

Before antibiotic drugs were available, death rates of 80% were reported by various authors; the present series was too small to justify any conclusion as to mortality, but in the authors' view it cannot be doubted that it has been lowered. Streptomycin is the drug of choice, with chloramphenicol a useful second. The mean age of the patients is usually high (48·7 years according to Solomon (*J. Amer. med. Ass.*, 1937, **108**, 937)) and the incidence is much higher in men than in women, ratios of 7 : 1 and 5 : 1 being noted in two reported series. The authors' 3 patients were all men of late middle age. The authors estimate the incidence of Friedländer pneumonia at about 1% of all cases of pneumonia.

Charles McNeil

460. **Role of the Friedländer Bacillus in Chronic Respiratory Disease**
J. K. FULTON and B. C. MCKINLAY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **40**, 245–248, Feb., 1954. 5 refs.

461. **Antibiotic Prophylaxis in Chronic Respiratory Diseases**
L. V. MCVAY and D. H. SPRUNT. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 833–846, Dec., 1953. 1 fig., 32 refs.

To assess the value of the long-term administration of aureomycin (chlortetracycline) in the prophylaxis of recurrent infection in cases of chronic respiratory disease an investigation was carried out in which 29 patients with chronic bronchitis associated with bronchiectasis, emphysema, or asthma, and one with chronic otitis media participated. Aureomycin in a dose of 0·25 g. twice daily was given for an average period of 11 months to 21 of the patients, while the remainder received dummy capsules and were observed as controls for an average period of 7·7 months. During the observation period one patient in the treated group died of cardiac failure without evidence of added acute infection, and one in the control group died of bronchopneumonia. The treated patients experienced fewer incidents of acute respiratory infection, and a larger proportion of them stated that they felt better. Four of the treated patients had some diarrhoea, which was severe in only one case, and 2 had mild pruritus ani; these were the only important side-effects. No very striking changes occurred in the bacterial flora of the sputum; no resistant strains of pathogenic bacteria emerged. [*Haemophilus influenzae* is not mentioned as having been isolated at any time.] No important increase in the incidence of *Candida albicans* was found; this was attributed to the inclusion of methyl and propyl esters of *p*-hydroxybenzoic acid [quantity not stated] in the capsules of aureomycin.

[Although it is claimed that "neither the patient nor the physician knew which preparation a given person

was receiving", it is also stated that "because of the patient's condition and as a result of requests by physicians, 21 patients were included in the . . . treated and only 9 in the . . . control series". The validity of the controls is thus open to question.] *J. G. Scadding*

462. **Bronchiectasis Due to Aspergilloma**
G. D. PESLE and O. MONOD. *Diseases of the Chest* [*Dis. Chest*] **25**, 172–183, Feb., 1954. 10 figs., 13 refs.

A special form of pulmonary mycosis is described, characterized by the presence of a mycelial tumour due to *Aspergillus* in a distended bronchus, with recurrent haemoptysis and a peculiar radiographic appearance, there being a uniform, rounded, moderately dense opacity surmounted by a thin, clear crescent. It is thought more probable that the associated bronchial dilatation is secondary to the infection than that the aspergillus grows in an already abnormal bronchus. Three new cases and 6 previously reported ones are described.

[Broncho-pulmonary aspergillosis has been extensively reviewed by Hinson *et al.* (*Thorax*, 1952, **7**, 317), who also described 3 cases of "mycetoma". Their paper is not quoted by the authors.] *J. R. Bignall*

463. **Pulmonary Blastomycosis. The Influence of the Immunologic Findings on the Selection of Patients for Operation**
W. C. SEALY, J. P. COLLINS, and E. E. MENEFEE. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 238–243, March, 1954. 4 figs., 5 refs.

See also Pathology, Abstract 306.

464. **Occupations and Cigarette Smoking as Factors in Lung Cancer**
L. BRESLOW, LEM. HOAGLIN, G. RASMUSSEN, and H. K. ABRAMS. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 171–181, Feb., 1954. 14 refs.

In this investigation, carried out on behalf of the California State Department of Public Health during the period 1949–52, the authors adopted a retrospective method similar to that which has been used by other workers in Great Britain, Finland, and the U.S.A.—that is, they compared the smoking histories given by patients with cancer of the lung with those given by control subjects with other diseases (in this case excluding patients with other forms of cancer and with other chest diseases). For each patient with cancer of the lung a control subject was selected of the same sex and age and admitted to the same hospital at about the same time. Information was obtained from 518 patients in each group concerning the amount and method of smoking, the age at starting, the habits of inhaling and of smoking before breakfast, and the presence or absence of a "cigarette cough".

Analysis of the results showed that there was a strong association between occurrence of the disease and cigarette smoking, but no clear association with the consumption of other tobacco products. The association was more marked for squamous and undifferentiated types of cancer than for adenocarcinoma. Estimates of the risk involved in smoking calculated from these data are similar to those calculated by other American and by British workers, the most notable discrepancy between the results of this and the British investigation being the finding of a higher proportion of "inhalers" among the cigarette smokers in the group with cancer.

The nature of all occupations pursued for at least 5 years by these patients and controls, classified according to the U.S. Employment Service Scheme, were also recorded and their distribution in the two groups compared. Few occupations had been followed by any appreciable number of men, and it is thus not possible to be confident that differences between the groups are significant; 13 occupations are, however, listed which occurred at least twice as frequently among the patients with cancer of the lung. When the occupations were grouped according to possibly significant exposure it was found that 7 such groups were excessively represented in the cancer group; the difference was statistically significant (after allowing for differences in smoking habits) only for welders (14 cases in the cancer group, 2 controls), and on the borderline of significance for men brought into contact with asbestos (10 cases in the cancer group, 1 control). *R. Doll*

465. **Primary Carcinoma of the Lung. Results of Surgical Treatment**
M. M. J. BREA. *Surgery* [*Surgery*] **35**, 167–173, Feb., 1954. 5 refs.

The author reviews a personal series of 200 cases of pulmonary resection performed at the University of Buenos Aires Medical School. These cases formed part of a total of 880 cases of cancer of the lung, of which 311 underwent thoracotomy, treated between 1944 and 1952. During this period the operability rate improved from 13 to 22%, and the resectability rate from 40 to 64%. The over-all operative mortality for pneumonectomy was 22%, while that for lobectomy was only 4·8%, these rates being directly correlated with the extent of the lesion and with the extent of operative intervention necessary for its correction. For small peripheral tumours, without lymph-node involvement and with free fissures, lobectomy was preferred.

Of the total, 150 patients survived the critical operative period; of these, subsequent recurrence led to the death of 92, while 58 survived. The author points out that 81 of the 92 deaths occurred within 2 years of operation, only 11 patients dying in the following 2 years, and he believes that patients who outlive this critical period have a good chance of permanent cure. Out of 125 patients treated more than 4 years ago, 34 have survived —9 (42·8%) of the 21 treated by lobectomy and 25 (24%) of the 104 treated by pneumonectomy; from this the author concludes that surgical treatment may be expected to give a 5-year survival rate of about 25%. Histological classification of the tumour, which was possible in 185 cases, revealed that 55·1% were epidermoid (squamous celled), 31·3% adenocarcinoma, 9·2% undifferentiated, and 4·7% miscellaneous (including 5 cases of sarcoma). The undifferentiated tumours were found mostly in the inoperable group, the adenocarcinomata were treated

mainly by lobectomy, and the squamous-celled growths by pneumonectomy.

The author's conclusions relating to mortality and survival are as follows: (*a*) the operative risk rises with extrapulmonary extension of the lesion and the more radical excision required to effect its removal; (*b*) the prognosis is less dependent on the histology of the tumour and type of operation than on the extent of spread of the growth; (*c*) the aim of physicians and surgeons dealing with the problem of bronchogenic carcinoma should be to concentrate on methods of earlier diagnosis rather than on devising methods of wider operation.

C. A. Jackson

466. **Metastatic Tumors of the Brain and Their Relation to Primary and Secondary Pulmonary Cancer**
E. M. KNIGHTS. *Cancer* [*Cancer* (*N.Y.*)] **7**, 259–265, March, 1954. 3 figs., 42 refs.

467. **Atony and Expiratory Invagination of the Membranous Part of the Intrathoracic Trachea and Main Bronchi as the Cause of Asphyxial Attacks in Bronchial Asthma and the Chronic Spasmodic Bronchitis of Emphysema.** (Erschlaffung und exspiratorische Invagination des membranösen Teils der intrathorakalen Luftröhre und der Hauptbronchien als Ursache der asphyktischen Anfälle beim Asthma bronchiale und bei der chronischen asthmoiden Bronchitis des Lungenemphysems)
H. HERZOG. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **84**, 217–221, Feb. 13, 1954. 4 figs., 20 refs.

The author describes 5 cases of chronic spastic bronchitis and emphysema which in addition showed a syndrome characterized by respiratory obstruction. The components of this syndrome were expiratory stridor (in 3 cases), asphyxial attacks (3), uncontrollable irritating cough (3), and severe dyspnoea (in all 5). Because of these symptoms the patients were examined by bronchoscopy at the University Clinic, Basle. Obstruction was found to be due to ballooning of the membranous part of the trachea and main bronchi into the lumen during expiration. In 4 of the cases this left only a narrow, slit-like passage which sometimes became obstructed by mucus, and in one case obstruction became complete. The mucosa appeared red and sometimes swollen, while the longitudinal striation of the membrane had disappeared. The cartilages were not unduly mobile and appeared to be normal in all but one case, in which they were seen to be flattened antero-posteriorly. During inspiration the lumen returned to approximately its normal size.

The author suggests that the invagination is caused by increased intrapulmonary pressure during expiration, forcing the atonic membrane into the trachea. Once the lumen has become narrowed a suction effect is produced, thus increasing the invagination. Contact between the walls acts as a stimulus for the coughing.

In one of the cases described, in which symptoms were particularly severe, operative treatment was carried out. A thin plate of bone was placed over the posterior aspect of the membrane and fixed in position with interrupted silk sutures encircling the bone and running between the cartilages in the submucosal plane of the membrane. Following this procedure there was marked improvement, the trachea remaining widely open during expiration.

[The author of this interesting article gives the impression that he believes this to be the only mechanism involved in causing expiratory obstruction and appears to discount the significance of bronchial spasm. Not everyone will be prepared to accept this view on the evidence of five cases, nor are the two mechanisms necessarily exclusive of each other.] *F. Starer*

468. **Pulmonary Hypertension. III. Physiologic Studies in Three Cases of Carbon Dioxide Narcosis Treated by Artificial Respiration**
F. W. LOVEJOY, P. N. G. YU, R. E. NYE, H. A. JOOS, and J. H. SIMPSON. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 4–11, Jan., 1954. 3 figs., 19 refs.

In patients with chronic pulmonary emphysema and severe hypercapnia associated with hypoventilation the respiratory centre becomes adapted to the high arterial carbon dioxide tension. In such cases the control of breathing is provided to a large extent only by the effects of anoxia on the carotid and aortic bodies. When oxygen is administered to these patients a vicious circle is started —the anoxic stimulus being removed, there is increased hypoventilation and carbon dioxide retention and coma result—and treatment is therefore a difficult problem.

The authors have recently treated 3 such patients by artificial respiration in a Drinker body respirator at Rochester (New York) Municipal Hospital. Lung volume studies showed that 2 of the patients suffered predominantly from pulmonary fibrosis; both recovered and now have less respiratory distress than before admission; in one case a pharyngeal airway had to be introduced, while the other patient had initial difficulty in synchronizing her breathing with the respirator. The third patient, who had severe emphysema, died despite treatment in the respirator. It is considered probable that the first 2 patients would not have survived long without this treatment.

Before treatment, all 3 patients had severe dyspnoea, cyanosis, and tachypnoea at rest, and administration of oxygen had caused coma. Observations made during the course of treatment, which included measurement of oxygen consumption, serial arterial blood gas analyses, and determination of the blood *p*H, showed that there was severe hypercapnia, hypoxaemia, respiratory acidosis, and polycythaemia in all cases. Artificial respiration in the respirator for 9 or 10 days was required before there was stable chemical improvement. Cardiac catheterization in one case before therapy showed severe pulmonary hypertension, with marked hypoxaemia, hypercapnia, and respiratory acidosis, but after treatment catheterization in each case showed moderate pulmonary hypertension and increased pulmonary resistance associated with a normal cardiac index. Even after respiratory acidosis had been neutralized, several days were required for the respiratory centre to become adjusted to the relatively normal arterial carbon dioxide tension. *D. Goldman*

PLEURA

469. **The Clinical and Cytological Investigation of Pleural Effusion**

R. F. ROBERTSON. *Edinburgh Medical Journal* [*Edinb. med. J.*] **61**, 37–49, Feb., 1954. 9 figs.

In this paper the author discusses his experience of the various types of pleural effusion. Of 236 cases of primary tuberculous pleural effusion seen in the 5-year period 1947–52, 24 occurred in patients over the age of 40, and these cases are compared in their clinical aspects with 24 cases of pleural effusion, also in patients over 40, which subsequently proved to be due to the presence of malignant disease in the lung or elsewhere, but which had originally been classified as of unknown aetiology. The chief differences were, in the neoplastic group, less frequent presence of pyrexia and pain and a greater incidence of haemoptysis, clubbing of the fingers, recurrence of fluid after aspiration, blood-staining of the effusion, and of history of an antecedent period of ill-health. Direct examination of the effusion for tubercle bacilli is nearly always useless, but attempts to culture the organism were felt to be worth while, in spite of the delay entailed—but only if performed on at least 10 specimens.

Similar types of effusion are described, such as those due to myocardial infarction, pulmonary infarction, systemic lupus erythematosus, and Brill–Symmers disease (lymphoid follicular reticulosis), and those occurring after therapy for bacterial pneumonia. Cytological investigation of the pleural fluid and differential leucocyte counts are discussed, with descriptions of the different types of cell encountered. In searching for malignant cells the author has found that embedding the centrifuge deposit in paraffin wax and cutting sections is the most reliable method. Although in his series only 24% of all malignant effusions could be diagnosed with absolute certainty by cytological examination, the author considers the method worth while as a possible aid to the solution of an often difficult diagnostic problem.

R. Heptinstall

470. **The Production of Pleural Adhesions by Kaolin Injection**

J. MAXWELL. *Thorax* [*Thorax*] **9**, 10–13, March, 1954.. 12 refs.

In the author's opinion a spontaneous pneumothorax is likely to be recurrent in over 50% of cases, most estimates being misleadingly low because the observation period on which they are based is too short. He suggests, therefore, that pleurodesis should be considered when pneumothorax is first diagnosed. The history of pleurodesis is reviewed briefly, and the relative efficacy and disadvantages of the substances in common use are discussed. Kaolin is considered to be superior to either silver nitrate or talc, which are probably the most popular substances in common use. It is not so violent in local or general effect as the former, nor has it the latter's propensity to form granulomata.

After some trial, 2 ml. of 25% suspension of kaolin in distilled water was found to produce satisfactory pleurodesis. The suspension is easy both to sterilize and to inject intrapleurally. Where the degree of collapse is great, withdrawal of air may help, but in most cases this is not necessary. Pain, shock, and fever are of only moderate severity, and aspiration of the reactionary pleural effusion is never necessary. This method has been used in 23 cases at the Royal Chest Hospital, London, since 1951, and there has been no recurrence on the treated side. Analysis of samples of effusion withdrawn on the 8th day showed in 2 cases that there had been considerable absorption of the aluminium fraction of the kaolin, whereas in 3 cases the ratio of aluminium to silica was unaltered.

J. N. Harris-Jones

MEDIASTINUM

471. **Bilateral Hilar Lymphadenopathy. Its Association with Erythema Nodosum**

N. WYNN-WILLIAMS and G. F. EDWARDS. *Lancet* [*Lancet*] **1**, 278–281, Feb. 6, 1954. 5 figs., 7 refs.

At the Bedford Chest Clinic and General Hospital which serve a population of about 150,000, 17 cases of bilateral enlargement of hilar lymph nodes were seen between 1947 and 1953. The clinical and laboratory findings in these cases are compared with those observed in 15 patients with presumed sarcoidosis and in 49 with erythema nodosum without bilateral hilar adenopathy, all of whom were seen during the same period, in order to discover whether any relationship exists between these three conditions.

Of the 17 patients with bilateral hilar lymphadenopathy, 12 also had erythema nodosum, 7 polyarthritis, 4 iridocyclitis or chronic angular conjunctivitis, and 3 enlarged superficial lymph nodes. Only one gave a positive tuberculin reaction to 1 t.u. (tuberculin unit), and 4 did not react to 100 t.u. The diagnosis of sarcoidosis was reached on clinical evidence alone in all but 2 of the 15 cases. Erythema nodosum was present in 2 of these 15, ocular signs in 4, enlarged superficial lymph nodes in 7, and other skin lesions in one. On tuberculin skin testing there was a positive reaction to 1 t.u. in one case and a negative reaction to 100 t.u. in 4 cases. On the other hand, of the group of 49 patients with erythema nodosum unaccompanied by hilar-node enlargement, 26 gave a positive reaction to 1 t.u. and 9 a negative reaction to 100 t.u. Evidence of tuberculosis was found in 22 of the 49 patients, but none had polyarthritis, ocular lesions, or enlarged superficial lymph nodes.

It is concluded from this investigation that bilateral hilar lymph-node enlargement, with or without erythema nodosum, is probably caused by the agent responsible for sarcoidosis, which condition is not so rare in Britain as has hitherto been thought.

[Bilateral hilar lymph-node enlargement without obvious lung changes is a well-recognized manifestation of histologically confirmed sarcoidosis. Slight changes in the lung fields were observed in 6 of the 17 patients with hilar lymphadenopathy, and of the 15 patients in whom sarcoidosis was diagnosed, 9 had enlarged hilar or mediastinal lymph nodes.] *J. R. Bignall*

Endocrinology

472. **Comparative Renal Responses to Water and the Antidiuretic Hormone in Diabetes Insipidus and in Chronic Renal Disease**
A. G. WHITE, M. KURTZ, and G. RUBIN. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 220–230, Feb., 1954. 4 figs., 22 refs.

The diminished ability of the cells of the distal tubules of the kidney to reabsorb water in cases of diabetes insipidus being due to deficiency of the pituitary antidiuretic hormone, it is suggested that the similar tubular dysfunction present in some cases of chronic renal disease may be due to inability of the tubular cell to respond normally to the hormone. In order to investigate this theory, experiments were carried out at the Mount Sinai Hospital, New York, on 4 patients with diabetes insipidus and 5 with chronic glomerulonephritis or pyelonephritis. An infusion of 5% glucose solution, which normally causes a rise in the rate of urinary excretion, had no such effect in either group and even caused a reduction in the rate of flow in some of the patients with diabetes insipidus, who were excreting initially at a higher rate than those with renal disease. Similar results were obtained in the latter after the ingestion of water. The intravenous injection of vasopressin inhibited water diuresis for a shorter time in both groups of patients than in normal subjects. Serum levels of sodium, potassium, and chloride were normal initially in both groups, and neither the infusion of 5% glucose nor the injection of vasopressin had any significant effect on them in the patients with diabetes insipidus; in 3 of the patients with renal disease the serum concentration of sodium was reduced at the time of maximum antidiuretic response to vasopressin, but no other disturbance of serum or urinary electrolyte levels was observed. It is suggested that patients with chronic renal disease may be considered to have a type of diabetes insipidus affecting the end-organ, in contrast to the usual type, which is central in origin.

A. C. Crooke

473. **Aphonia and Deafness in Hyperparathyroidism**
J. A. SIMPSON. *British Medical Journal* [*Brit. med. J.*] **1**, 494–496, Feb. 27, 1954. 2 figs., 22 refs.

The role of calcium in producing variations in the excitability of nervous tissue is generally accepted. The author reports, from the Gardner Institute of Medicine, University of Glasgow, 3 cases of hyperparathyroidism in all of which deafness occurred preoperatively and in one case was associated with aphonia. These symptoms tended to vary with the degree of muscular weakness. In all 3 cases there was no recurrence of the deafness after removal of an adenoma of the parathyroid. Two other cases occurred, but these 2 patients could not be traced for follow-up examination.

The author reviews the literature relating to the occurrence of sensory manifestations in hyperparathyroidism, and suggests that the decreased nerve excitability due to a high level of ionized calcium in the blood, which is thought to be the cause of motor weakness, may also be the cause of deafness and other sensory manifestations. He tested this hypothesis in one case by studying the "time-constant of accommodation" of the ulnar nerve in response to an electric stimulus (the method of Solandt (*Proc. roy. Soc. B.*, 1936, **119**, 355), the index of excitability of a nerve having been shown to be lowered by increasing the amount of calcium in the environment of the nerve). The test showed that the sensory nerve accommodation was greatly increased in this case.

Nigel Compston

THYROID GLAND

474. **Measurements of Absolute Radio-iodine Uptake in the Assessment of Human Thyroid Activity**
C. P. HAIGH, M. REISS, and J. M. REISS. *Journal of Endocrinology* [*J. Endocr.*] **10**, 273–283, March, 1954. 6 figs., 14 refs.

The authors, working at the Bristol Mental Hospitals, have devised a method of measuring the 24-hour uptake of radioactive iodine (^{131}I) by the human thyroid gland by means of a special toroidal counter. This counter is in the form of a ring with a mean diameter of 18 cm. which slips over the patient's head and encircles the neck at the level of the thyroid gland. The advantages claimed for it are that it is uniformly sensitive over its whole circumference, so that the counting rate is not altered appreciably by movements of the patient's head, and that its sensitivity is such that a dose of 5 μc. of ^{131}I is sufficient for test purposes.

The 24-hour thyroid uptake of ^{131}I in 297 male and 293 female subjects was determined and correlated with urinary excretion over 24 or 48 hours, the sum of the two values averaging 91% of the dose. The rate of uptake during the first hour after administering the dose was also determined, and was found in some cases to be subnormal although the 24-hour uptake of ^{131}I was normal or slightly raised. This discrepancy occurred chiefly in patients suffering from anxiety neurosis. In experiments on anaesthetized rabbits it was found that the intravenous administration of 0·1 mg. of adrenaline diminished the thyroid uptake of ^{131}I. It is therefore suggested that in these over-anxious patients the stress of attending for an examination may have caused the mobilization of vasoconstrictor substances during the earlier stages of the investigation.

G. Ansell

475. **Observations on a Relationship between Total Thyroid Iodine Content and the Iodide-concentrating Mechanism of the Thyroid Gland of the Rat**
W. P. VANDERLAAN and R. CAPLAN. *Endocrinology* [*Endocrinology*] **54**, 437–447, April, 1954. 4 figs., 11 refs.

476. **Myxoedema and Basophil Adenomata of the Pituitary Gland.** (Myxœdème et adénomes basophiles de l'hypophyse)
L. LANGERON, P. GIARD, and G. VINCENT. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. méd. (Paris)*] **138**, 79–83, 1954. 1 ref.

The cases are reported of 2 women, aged 46 and 68 respectively, in whom the slow development of symptoms of cardiac failure and myxoedema terminated in a fatal cardiac collapse. Necropsy showed extensive atrophy of the thyroid gland and a basophil adenoma of the pituitary gland in both cases. The primary condition was considered to be a thyroid degeneration of unknown origin leading to overstimulation of the pituitary and consequent development of the adenoma.

F. W. Chattaway

477. **Development of Goiters in Cretins without Iodine Deficiency: Hypothyroidism Due to Apparent Inability of the Thyroid Gland to Synthesize Hormone**
L. WILKINS, G. W. CLAYTON, and M. BERTHRONG. *Pediatrics* [*Pediatrics*] **13**, 235–246, March, 1954. 6 figs., 10 refs.

In endemic cretinism a normal thyroid gland is deprived of iodine and responds by hypertrophy, forming a goitre. In most cases of sporadic cretinism, however, the condition is due to an absence of active thyroid tissue or grave dysfunction of the thyroid gland, and goitre does not result. Yet in 1897 Osler reported that of 60 cases of sporadic cretinism occurring in the United States, 7 were associated with goitre in the absence of iodine deficiency.

In the present paper the authors describe 4 cases of this type which were identified in a study of 115 cases of sporadic cretinism seen at Johns Hopkins Hospital, Baltimore. Investigations with radioactive iodine (^{131}I) showed that the uptake of iodine was normal and that the essential defect is therefore an inability of the gland to utilize iodine in the synthesis of thyroxine. The point at which the synthesis breaks down has not been determined and it is possible that it varies from case to case. Although the thyroid gland is originally normal in size, persistence of hypothyroidism causes the gland to hypertrophy owing to the action of pituitary thyrotrophin, and the patients develop goitre unless they are effectively treated at an early stage. There is thought to be a familial element in this type of hypothyroidism which the authors believe is commoner than is realized.

T. A. A. Hunter

478. **Iodothiouracil in Treatment of Toxic Goitre**
H. J. B. GALBRAITH, D. F. E. NASH, and A. W. SPENCE. *British Medical Journal* [*Brit. med. J.*] **1**, 420–422, Feb. 20, 1954. 17 refs.

The authors report the clinical trial at St. Bartholomew's Hospital, London, of sodium iodothiouracil (" itrumil ") in the treatment, preparatory to operation, of 23 patients suffering from hyperthyroidism. The drug was given in doses of 200 (later 300) mg. daily for periods of 12 days to 7 months, the higher dosage being generally found the more satisfactory. Of the 23 patients, 18 subsequently underwent thyroidectomy after reduction of the hyperthyroidism, the goitre showing evidence of involution. The results of prolonged medical treatment in the other 5 were variable. In a further group of 6 hyperthyroid patients given preoperative treatment with methylthiouracil and potassium iodide concurrently. the results obtained were equally satisfactory, indicating that the pharmacological properties of iodothiouracil differ little from those of iodine and thiouracil administered together.

F. W. Chattaway

479. **Long-term Therapy of Thyrotoxicosis with Thiouracil Compounds**
J. F. GOODWIN, H. STEINBERG, and A. WILSON. *British Medical Journal* [*Brit. med. J.*] **1**, 422–425, Feb. 20, 1954. 3 figs., 11 refs.

On the basis of the long-term results of a study begun at Sheffield Royal Infirmary in 1944, the methods used in which, and some early results, have already been described (*Lancet*, 1947, **1**, 669; *Abstracts of World Medicine*, 1947, **2**, 524), the authors discuss (1) the value of thiouracil compounds in the initial control of thyrotoxicosis, (2) to what extent control can be exercised over long periods by maintenance doses of the drugs, and (3) the likelihood of relapse after maintenance therapy is withdrawn.

Of the 126 thyrotoxic patients included in the study, initial control was obtained in 113 (90%) after 3 to 6 weeks' treatment, and of these, 105 were successfully kept in remission by maintenance doses of the compounds for periods of 3 to 62 months (mean, $18 \pm 12{\cdot}9$ months). Then, after 2 to 55 months (mean 17·1 months) of satisfactory remission, therapy was withdrawn in 94 of these cases, with the result that 55 eventually relapsed at various times after withdrawal, but 39, at the time of the last interview [not stated], were still in remission after periods ranging from 3 to 47 months. The probability of relapse was greatest within about 15 months of withdrawal of therapy, and least 36 months after withdrawal. No correlation was found between the length of the remission and the patient's age, duration of illness, or duration of treatment. *F. W. Chattaway*

480. **The Diagnosis of Thyrotoxicosis**
E. J. WAYNE. *British Medical Journal* [*Brit. med. J.*] **1**, 411–419, Feb. 20, 1954. 7 figs., bibliography.

In this paper, delivered as the Bradshaw Lecture to the Royal College of Physicians of London, the author reviews his experience of the value of clinical signs and symptoms and of special tests of thyroid function in the diagnosis of thyrotoxicosis. Basing his conclusions on examination of 90 patients with toxic and 72 with nontoxic goitre and 90 controls, comparable as to age and sex, seen in recent years at Sheffield Royal Infirmary, the author asserts that the presence of the classic signs and symptoms of thyrotoxicosis is a reliable diagnostic guide in males but not in females, especially women at the menopause. The most helpful and constant diagnostic features are increased appetite, persistent tachycardia especially during sleep, loss of weight, preference for cold weather, sweating hands, and hyperkinesis.

The author also discusses the relative advantages and disadvantages of tests with radioactive iodine (^{131}I), and the value of estimation of the basal metabolic rate and of the serum protein-bound iodine content as indicators of thyroid function. The radioactive-iodine tests employed were determination of uptake of ^{131}I by the thyroid gland after 4 hours, estimation of the protein-bound plasma radioactivity after 48 hours, blood clearance of ^{131}I by the thyroid gland, and urinary excretion of ^{131}I. The first two tests were found to be the most satisfactory, and if only one of them can be employed, then estimation of protein-bound plasma activity (as an index of the amount of circulating thyroxine) is considered the better test to use for distinguishing between toxic and non-toxic cases. The author reminds us that these tests must be interpreted with caution if treatment involving the administration of iodine-containing compounds or of thiouracil has been given shortly before the test. The determination of the serum protein-bound iodine level is also of diagnostic value, but is technically too difficult for routine use, while reported results have shown considerable variation. The determination of the serum creatine level and the leucocyte count are not of value diagnostically. The psychological features of the disease are often of considerable importance in the management of the case, but are of little or no assistance in the establishment of a diagnosis.

F. W. Chattaway

481. **The Effects of L-Triiodothyronine and L-Thyroxine on the Metabolism of Tissues *in vitro***

J. G. Wiswell, K. L. Zierler, M. B. Fasano, and S. P. Asper. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **94**, 94–104, Feb., 1954. 27 refs.

Although there is an acceleration of oxygen uptake by isolated tissue from animals treated with desiccated thyroid or thyroxine, it has never been shown conclusively that thyroxine can stimulate the oxygen consumption of isolated normal tissues when applied to them *in vitro*.

In experiments carried out at Johns Hopkins University School of Medicine, liver slices and hemidiaphragms from normal rats were incubated with and without L-triiodothyronine in the incubating medium. The compound had no significant effect on the oxygen uptake, which gradually fell during the 8 hours of observation. The oxygen uptake of tissues from hypothyroid rats treated with L-triiodothyronine or L-thyroxine was raised about 50% above that of tissue from untreated control hypothyroid animals. The former compound tended to have the greater effect, the difference not being due to greater relative dosage.

Further experiments showed that L-triiodothyronine had a more intense but less prolonged effect than L-thyroxine in stimulating the oxygen utilization of the homogenate–cytochrome-C–succinate system of the rat heart. The activation did not occur if addition of the hormone was delayed until after one hour of incubation. The authors are as yet unable to offer any satisfactory explanation of these findings, but a number of interesting hypotheses are discussed. *C. L. Cope*

ADRENAL GLANDS

482. **The Action of Electrocortin in the Adrenalectomized Dog.** [In English]

F. Gross and H. Gysel. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **15**, 199–209, March, 1954. 7 figs., 15 refs.

At the Ciba Research Laboratories, Basle, 4 male dogs which had been adrenalectomized one to two years previously were maintained in good health by the subcutaneous injection of 0·7 to 1·0 mg. of deoxycortone acetate once daily. This substance was then replaced by "electrocortin" (now renamed aldosterone), a recently isolated amorphous fraction of adrenal extract first reported by Simpson *et al.* (*Experientia*, 1953, **9**, 333), with equally good results. Only 1·5 to 2·0 μg. of electrocortin per kg. body weight was required for maintenance, and its potency is therefore regarded as 25 to 30 times that of deoxycortone acetate. Because of limited supplies it was not possible to extend the maintenance test for more than 10 days, and the long-term action of the new substance could not therefore be investigated.

When the change from deoxycortone acetate to electrocortin was effected, the haemoglobin concentration and serum non-protein nitrogen level of the dogs increased slightly and remained at this higher level; excretion of urine, sodium, and chloride showed a transient rise, representing the disappearance of the hydraemia which exists in the adrenalectomized dog maintained on deoxycortone acetate. The excretion of water, as determined by water loading tests, was delayed in a manner similar to that which occurs with deoxycortone acetate. In this respect electrocortin differs from cortisone, in the presence of which water excretion is normal under the same experimental conditions. Overdosage of electrocortin, however, in contrast to deoxycortone acetate, does not produce marked retention of water, sodium, or chloride. *H. Herxheimer*

483. **Effects of ACTH on Mental Function**

S. Malitz, D. A. Hamburg, and S. Modell. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **118**, 315–331, Oct., 1953 [received March, 1954]. 36 refs.

The authors, after briefly reviewing previous reports of the effect of ACTH on mental function and in causing behavioural changes, describe an experiment carried out at the Walter Reed Army Medical Center, Washington, D.C., in which 11 unselected young male patients with acute hepatitis, 5 of whom were receiving ACTH as part of their treatment, were given psychological tests before treatment began, between the 12th and 18th days (since this appeared to be the time when the effects of ACTH would be at their maximum), and after the end of treatment. The other 6 patients acted as controls. Each patient was interviewed by a psychiatrist before medication and 2 or 3 times per week thereafter, observations being made on the patient's appearance, motor activity, mood, and behaviour. The total dose of ACTH ranged from 155 to 248 mg. given over periods varying from 2 to 30 days.

The results [discussed at a length hardly justified by the very small number of cases] were entirely inconclusive, no definite change being noted in the patients who received treatment with ACTH, nor any difference between these 5 patients and the 6 in the control group. The authors therefore conclude that "the strikingly uniform lack of major psychologic changes suggests that the central pharmacologic action of ACTH on the central nervous system has no specific effect on mood and behaviour when administered in the usual clinical dosages." *John C. Kenna*

484. **The Psychiatric Risk from Corticotrophin and Cortisone**
A. LEWIS and J. J. FLEMINGER. *Lancet* [*Lancet*] **1**, 383–386, Feb. 20, 1954. 15 refs.

In order to test the thesis that cortisone and corticotrophin (ACTH) should not be given to patients with evidence of psychopathic personality, the authors studied 12 patients at the Maudsley Hospital, London, each of whom had a physical disease which might be relieved by these drugs and had also had an unequivocal mental illness. Eleven of the patients had rheumatoid arthritis and one disseminated lupus erythematosus, and their psychiatric history indicated a severe degree of abnormality, including such conditions as obsessional neurosis, conversion hysteria, schizophrenia, and involutional depression.

After a control period of 6 weeks a placebo was given for 10 days, followed by corticotrophin or cortisone in increasing doses, starting with 40 to 60 mg. of the former and 100 mg. of the latter in 24 hours, until the maximum physical benefit had been obtained, the drug then being withdrawn slowly. The patients' physical condition responded as expected to the drug and relapsed during its withdrawal, while their mental condition improved concomitantly with the physical and relapsed at the same time; in fact the mental improvement seemed to be due to a psychological reaction (normal or hysterical) to the physical improvement rather than to a direct pharmacological effect. The findings of psychological tests before and during treatment provided no decisive evidence of cognitive or emotional changes.

It is concluded, therefore, "that predisposition to develop untoward mental symptoms under treatment with corticotrophin or cortisone cannot be assumed in patients with unstable neurotic personality or a history of mental illness." *Oswald Savage*

485. **Adrenocortical Function in Burned Patients. With Special Reference to A.C.T.H. and Adrenaline Tests**
S. SEVITT. *British Medical Journal* [*Brit. med. J.*] **1**, 541–546, March 6, 1954. 7 figs., 20 refs.

The duration of the period of eosinopenia which follows burning was estimated to within $\pm\frac{1}{2}$ day in 35 cases at the Birmingham Accident Hospital, and was plotted against the area of skin burned. The eosinopenia lasted only 1 to 2 days when less than 10% of the body area was burned, but up to 5 days when larger areas were burned. Eleven patients died during the period of eosinopenia and it is concluded that in these cases the adrenal cortex remained hyperactive until the time of death. In 5 of the 7 other fatal cases there had been an initial period of eosinopenia of normal duration and there was no other evidence of adrenal failure; in one of the remaining cases the period of eosinopenia had been unduly short.

In 12 out of 14 patients tested the response of the eosinophil count to ACTH was normal in the post-eosinopenic period, and the response to adrenaline was likewise normal in 9 out of 12 patients tested. In neither of the 2 patients who responded abnormally to ACTH was the adrenocortical failure thus indicated considered to be serious, since one recovered and the other subsequently developed eosinopenia before death. Two of the 3 patients who responded abnormally to adrenaline responded normally to ACTH, indicating failure at the hypothalamic–pituitary level rather than adrenocortical failure. These patients were confused and irrational at the time of the abnormal response to adrenaline, the response becoming normal when mental recovery had taken place; it is therefore suggested that the mental disturbance and the lack of response to adrenaline were due to similar changes affecting the cerebral cortex and hypothalamus respectively.

It is recommended that severely burned patients should receive cortisone as soon as evidence of adrenocortical failure, in the form of either a premature return of the eosinophil count to normal or an abnormal eosinophil response to ACTH, is obtained.
C. L. Cope

486. **The Effect of ACTH and Cortisone on the Blood Pyruvic Acid Level.** [In English]
S. GITELSON. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **15**, 225–235, March, 1954. 4 figs., 33 refs.

See also Rheumatic Diseases, Abstract 500.

DIABETES MELLITUS

487. **Diabetic Angiopathy. A Specific Vascular Disease**
K. LUNDBÆK. *Lancet* [*Lancet*] **1**, 377–379, Feb. 20, 1954. 21 refs.

It is generally held that diabetes leads to specific vascular changes in the retina and kidneys and hastens the development of atherosclerosis. The author believes that all these vascular anomalies should be regarded as various manifestations of one generalized specific vascular disorder—a diabetic angiopathy. This opinion is based on a follow-up investigation of 234 unselected patients with diabetes of 15 to 25 years' duration who had been treated at the Kommunehospitalet, Aarhus, Denmark. Of this group, 165 patients were alive at the time of the follow-up, and detailed information was obtained on all but a few of those who had died. Diabetic retinopathy was found in 80% of the patients, occlusive vascular disease of the legs and signs of renal disease were both present in one-quarter of the patients, while heart disease was found exclusively in the elderly, two-thirds of the patients over 60 years of age being thus affected.

The clinical and histological pictures of coronary disease and of occlusive arterial disease of the legs do not differ from those seen in non-diabetics. Their incidence, however, was found to bear a relationship to the incidence of the specific vascular complications. For example, coronary disease was present in 69% of patients with renal disease compared with 30% of those without renal disease. Diabetic retinopathy was found in 88% of patients over 60 years of age with coronary disease compared with 56% of patients of like age without coronary disease. In this age group also occlusive vascular disease of the legs was present in 58% of patients with retinopathy, but in only 19% of those without retinopathy.

It is pointed out that vascular anomalies occur with about equal frequency in male and female patients with long-standing diabetes, in contrast to the known male–female ratio of 3 or 4 to 1 in non-diabetics. Small but significant differences are found between the lipid content of the coronary arteries in patients with long-standing diabetes and that in non-diabetics of similar age. Moreover, the serum phospholipid–cholesterol ratio, which is reduced in atherosclerosis, remains normal in young diabetics of long standing, although in old diabetic patients it is much the same as in non-diabetics. *K. O. Black*

488. **Degenerative Changes in Juvenile Diabetes Mellitus.** (Zur Erfassung degenerativer Veränderungen beim kindlichen Diabetes mellitus)
W. FALK and R. HINRICHS. *Österreichische Zeitschrift für Kinderheilkunde und Kinderfürsorge* [*Öst. Z. Kinderheilk.*] **9**, 362–371, 1954. 29 refs.

Children with diabetes show vascular complications relatively rarely and only after the disease has been established for several years, thus differing from the diabetic adult, in whom frequent and typical vascular complications, particularly of the eye and renal vessels, occur. But following certain personal observations the authors were led to speculate whether this difference was as great as has been thought, or whether it was not perhaps to some extent due to faulty or insufficiently sensitive techniques in examining for degenerative vascular changes in children.

With this in mind, therefore, they carried out the following investigations at the University Children's Clinic, Graz, on 26 diabetic children: (1) careful examination of the ocular fundi and of the refractory media of the eyes by means of corneal microscopy; (2) capillary resistance tests by the "suction-cup" method; (3) kidney function tests, in which tubular and glomerular performance was studied separately. Changes in the eye were found in 3 of the 26 patients. One 15-year-old girl, with diabetes of only 2 years' duration, had anterior and posterior cataract; a second girl, diabetic for 8 years, had severe myopia; and a boy with a 9-year history of diabetes and a typical Mauriac's syndrome had cataracta pulverulenta. Capillary resistance was greatly reduced in 15 patients, including the 3 with eye changes, and also a few cases in which the diabetes had been established only a year or two. The glomerular filtration rate, determined by the inulin clearance test, was found to be within normal limits in all but 2 patients. Five patients had occasional bouts of albuminuria, but in all these cases glomerular filtration and tubular resorption were normal. The 3 patients with eye changes also had normal kidney function.

The authors conclude that there can be no close connexion between reduced capillary resistance and the glomerular filtration rate, such as has been found by Spühler to exist in young diabetic adults. As the urea clearance level was found to be abnormally high in 4 children who later showed evidence of hypoglycaemia, they suggest that determination of urea clearance would provide a useful and sensitive test for latent hypoglycaemia in children. *Marianna Clark*

489. **Pyrimidine Metabolism in Diabetes Mellitus Studied with N^{15} Labeled Uracil**
R. CAREN and M. E. MORTON. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 141–148, Feb., 1954. 2 figs., 17 refs.

A hypothesis was advanced which assumes that diabetes mellitus may result as an error of pyrimidine metabolism which produces an alloxan-type substance at the isodialuric stage of the degradation of uracil. This would in turn affect the insulin producing cells of the pancreas to cause diabetes.

The pyrimidine uracil was synthesized with isotopic heavy nitrogen (^{15}N) and administered intravenously to a diabetic who did not receive insulin during the course of the study. The metabolism of the uracil was compared with a similar previous study in a normal man. It was shown that the uracil was broken down much more rapidly to urea in the diabetic than in the normal. However, only about 50% of the administered ^{15}N was recovered from the urine in both cases in the 72-hour period of investigation. An unidentified ^{15}N containing substance was excreted by the diabetic for a much longer period of time, 24 hours as compared to 8 hours for the normal. The urinary ammonia of the diabetic was found to contain the largest atom per cent excess of ^{15}N in the nitrogenous compounds which were identified in the urine.

The relation of the results of this study to the above hypothesis were discussed. The possibilities of uracil being broken down to urea by more than one route and that it might give rise to more end products than urea and ammonia were also discussed.—[Authors' summary.]

490. **The Insulin–Zinc Suspensions**
G. R. VENNING. *Lancet* [*Lancet*] **1**, 480–486, March 6, 1954. 8 refs.

A therapeutic trial of the insulin zinc suspensions was carried out at the Manchester Royal Infirmary on 34 patients (10 in-patients and 24 out-patients), the findings of which are here presented.

The claim that the insulin zinc suspensions exert a more reliable and even action on the blood sugar level than a mixture of protamine zinc and soluble insulins appeared to be substantiated. The majority of the patients studied were adults with the acute type of

diabetes, and required a larger dose of the insulin zinc suspension than of the preparation used previously, the increase in 5 cases being 50% or more. The diet was regulated to ensure that the carbohydrate was spread evenly throughout the latter part of the day, and it is stated that " a mid-afternoon meal is usually necessary, even when the main evening meal is taken as early as 6 p.m." Local allergic reactions were noted in 2 patients taking large doses of insulin zinc suspensions.

Although the author emphasizes that the time is not yet ripe to withdraw preparations such as protamine zinc insulin, his experience in this preliminary trial " suggests that acute diabetes can usually be controlled satisfactorily with a single daily injection of a suitable insulin-zinc suspension."

[This excellent report should be studied in the original by those wishing to adopt the insulin zinc suspensions.]

I. McLean Baird

491. **Insulin and Ketone Bodies.** (Insulina e corpi chetonici)

G. GAMBASSI and V. MAGGI. *Archivio di patologia e clinica medica* [*Arch. Patol. Clin. med.*] **31**, 77–87, 1954. 20 refs.

Working at the University of Bari, the authors studied the metabolism of the ketone bodies and its relation to insulin in 15 normal subjects, 10 patients suffering from diseases of the liver (ranging from " simple cholecystodystonia " to cancer of the liver), and 5 diabetics. All 30 were given a normal hospital diet before the test. The blood sugar concentration was estimated by the Hagedorn–Jensen method and the blood ketone content by the Engelfeldt–Pincussen method. After a specimen of blood had been taken for determination of the fasting blood sugar level, 10 subjects received 20 units of insulin, 5 received 10 units, and 6 received 5 units, intravenously in each case. The remaining subjects received insulin subcutaneously in doses of 15 to 70 units. Blood for examination was withdrawn every half-hour up to 90 minutes.

The results showed in general that the effect of insulin was to reduce the blood ketone level, but in certain cases this was followed by an increase in the β-oxybutyric acid fraction, which is attributed either to the secretion of adrenaline or to lack of glycogen in the liver.

E. Forrai

492. **The Effect of Intravenously Administered Fructose on the Ketone Bodies of the Depancreatized Dog**

P. WHITTLESEY and C. G. ZUBROD. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **110**, 226–231, Feb., 1954. 3 figs., 21 refs.

A study was carried out at Johns Hopkins School of Medicine, Baltimore, of the extent to which fructose, in the absence of insulin, can relieve the ketosis which is one of the results of insulin deprivation. Seven pancreatectomized dogs were given sufficient protamine zinc insulin daily to keep the level of glycosuria below 5 g. a day. Ketosis was then produced by depriving them of insulin for 4 to 10 days. The intravenous infusion of 3·4% glucose for 4 to 6 hours in unanaesthetized animals, along with 1·7 to 3·45 units of crystalline insulin intravenously per kg. body weight given at the start of the infusion, caused a rapid fall in the blood ketone-body concentration. The infusion of glucose alone, without insulin, did not affect the concentration of ketone bodies in the blood. When fructose in 10% solution was infused at rates varying from 1·6 to 3·34 g. per kg. body weight per hour for periods ranging from 2 to 8 hours, there was a fall in blood ketone-body concentration similar to that obtained with glucose plus insulin, but which continued only so long as the infusion lasted. This fall was not the result of urinary excretion of ketone bodies, and the authors point out that the estimation of ketone-body excretion in the urine does not adequately reflect changes in ketone-body concentration in the blood. (All the experiments were performed on unanaesthetized dogs with the aid of special apparatus, since barbiturate anaesthesia was found to block the effect of fructose and of glucose plus insulin on blood ketone-body levels.)

The authors conclude that fructose in the absence of insulin is ketolytic for short periods of time when administered to pancreatectomized, severely ketotic dogs.

P. A. Nasmyth

493. **Diabetogenic Action of Pancreatic Glucagon**

C. CAVALLERO, B. MALANDRA, and G. GALANSINO. *Nature* [*Nature (Lond.)*] **173**, 585–586, March 27, 1954. 1 fig., 4 refs.

Having previously investigated the diabetogenic effect of glucagon on forced-fed rats receiving a high-carbohydrate diet, the authors now report a similar study, carried out at the Institute of Pathological Anatomy, University of Milan, on intact, normally fed rats. The animals all received a standard diet and were divided into three groups, the first receiving subcutaneous injections of cortisone alone, the second glucagon alone, and the third a combination of both hormones. This treatment was continued for 20 days, but after 15 days glucose tolerance tests were performed and insulin sensitivity assessed in 10 rats from each group. At the end of the study period the animals were killed and histological sections made of the pancreatic tissue.

It was noted that, whereas body weight fell in the groups receiving cortisone or glucagon alone, it increased in the group given combined treatment. Glycosuria occurred also only in the group on combined treatment, in which the fasting blood sugar level was significantly higher than in the others. Glucose tolerance, which was largely uninfluenced by either cortisone or glucagon given separately, was reduced by a combination of the hormones. Histological examination of the pancreas showed that the α cells, the site of glucagon formation, were reduced in number in the animals given glucagon, either alone or in combination with cortisone.

From these results it would appear that glucagon alone is not diabetogenic, but can potentiate the diabetogenic action of cortisone. In discussing the mode of action of glucagon, which is still not well understood, the authors suggest that it may act either by increasing the release of glucose from liver stores or by inhibiting the peripheral action of insulin.

J. N. Harris-Jones

The Rheumatic Diseases

RHEUMATIC FEVER

494. ***para*-Acetylaminosalicylic Acid in the Treatment of Rheumatic Fever.** (L'acido para-acetilaminosalicilico nel trattamento della malattia reumatica)
F. BERTOLANI. *Minerva medica* [*Minerva med. (Torino)*] **1**, 567–576, Feb. 28, 1954. 11 figs., 25 refs.

As part of a study undertaken at the University of Modena of the relation between the delaying effect of certain drugs on erythrocyte sedimentation *in vitro* and their anti-rheumatic action, the anti-rheumatic effects of the N-acetyl derivative of *para*-aminosalicylic acid (APAS) have been studied. The authors have also carried out experiments, chiefly pharmacological, on this substance, on the diacetyl derivative (DAPAS) and on the acid itself (PAS). APAS has the greatest effect on erythrocyte sedimentation, DAPAS has a mild effect, and PAS has none.

APAS was used in the treatment of 8 cases of rheumatic polyarthritis in the acute phase, 7 of the patients being in hospital and one an out-patient, the dose varying from 10 to 25 g. daily. In 4 cases salicylates had been given previously without effect. In all cases the effect of APAS was to reduce the temperature and relieve the pain, while the signs of cardiac and respiratory distress abated. Signs and symptoms tended to recur if the drug was stopped too soon. When DAPAS was given the effects were the same, as was to be expected since, according to the authors, both DAPAS and PAS are transformed into APAS after ingestion to an extent which depends on a variety of circumstances.

Experimentally, both the sodium salt of APAS and sodium salicylate reduced artificially produced fever in rabbits, PAS being less reliable, but none of the PAS derivatives appeared to have any analgesic properties when tested on rats with infra-red radiation as the painful stimulus. It was shown that APAS (but not PAS) delayed the urinary excretion of phenolsulphonephthalein which had previously been injected into the talocrural joint of a rabbit; this property is found also in sodium salicylate and other anti-rheumatic substances.

The author considers that the conflict of opinion on the value of PAS in rheumatism may stem from the fact that its therapeutic effect depends on the degree of its conversion into APAS, which may vary from 30 to 85%.

J. G. Jamieson

495. **Dietary Eggs and Rheumatic Fever**
A. D. WALLIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 167–170, Feb., 1954. 10 refs.

Evidence is accumulating which supports the theory that rheumatic fever is caused by a tissue sensitivity reaction to some product of the Group-A β-haemolytic streptococcus. One of the two haemolysins produced by this organism, streptolysin S, is inhibited by a substance present in the serum of all individuals, sick or well, the inhibition being of a physico-chemical nature rather than an antigen–antibody reaction. The strength of this inhibiting substance varies from individual to individual, and is dependent in part on the concentration in the serum of phospholipid, one of the ingredients of which is choline. Since the body can neither synthesize nor store choline in any significant quantity, the serum phospholipid level must depend on the dietary intake of choline, by far the richest source of which is egg. The author therefore estimated the egg intake in childhood of 184 subjects with rheumatic heart disease and compared it with that of 1,380 unaffected persons interviewed at the Pennsylvania Hospital, Philadelphia. Of the affected subjects, 10·2% actively disliked eggs and 40·6% believed that their consumption of eggs in childhood had been relatively small, the corresponding figures being 4·6% and 16·3% respectively in the control group. It is suggested that this difference in probable choline intake might have a bearing on the difference in susceptibility to rheumatic fever between the two groups.

R. S. Illingworth

496. **Serum Phospholipid and Rheumatic Fever**
A. D. WALLIS and E. VIERGIVER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 171–178, Feb., 1954. 2 figs., 26 refs.

In a further study of the relation between the phospholipids in the serum and susceptibility to rheumatic fever [see Abstract 495] the authors determined the serum phospholipid level in 178 patients with inactive rheumatic heart disease. It was found that the level was below the average for normal individuals of the same age group in approximately two-thirds of these cases. Of 51 patients who had had more than one attack of rheumatic fever, 46 had either an abnormally low serum phospholipid level or a history of an unusually low intake of eggs in childhood.

It is suggested that rheumatic fever may be produced " when a hemolytic streptococcal infection engenders more streptolysin S than the natural serum inhibitor, as a reflection of serum phospholipid, is able to neutralize ".

R. S. Illingworth

497. **A Follow-up Study of Suspected Rheumatic Fever Patients**
C. M. MCCUE. *Journal of Pediatrics* [*J. Pediat.*] **44**, 290–293, March, 1954. 8 refs.

In the past 11 years 2,678 new patients have been seen in the Medical College of Virginia Rheumatic Fever Clinic. In this group, 236 were listed as " deferred " after a complete initial study. Follow-up data have been obtained on 209 of these 236 cases.

The complaints and suspicious signs which were the reason for deferral are listed and compared with those

[occurring in the 29 patients] later developing clear rheumatic fever. [This comparison shows a significantly higher incidence in the latter group of painful joints with swelling, fever, epistaxis, suspicious choreiform movements, increased erythrocyte sedimentation rate, electrocardiographic abnormality, and tachycardia.]

After an average follow-up period of 28 months, the following diagnoses have emerged:

Rheumatic fever .. .. .. (2·4% with rheumatic heart disease)	13·88%
Rechecked and no rheumatic fever or heart disease found	66·98%
Local medical doctor says no rheumatic fever	9·09%
Nurse says patient well	3·83%
Diagnosis still deferred after recheck	6·22%

The excellent prognosis in this group as a whole makes strict diagnostic criteria imperative.—[From the author's summary.]

498. **The Pathogenesis of Rheumatic Fever**
D. A. LONG. *Lancet* [*Lancet*] **1**, 529–537, March 13, 1954. 4 figs., bibliography.

See also Cardiovascular System, Abstracts 414 and 422.

CHRONIC RHEUMATISM

499. **Unrecognized Late Forms of Bechterew's Disease [Ankylosing Spondylitis].** (Unerkannte Spätformen der Bechterewschen Erkrankung).
G. MARTICKE. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **79**, 507–509, March 26, 1954. 3 refs.

This study was carried out at the Balneological Institute at Bad Nenndorf where, it is claimed, some 200 cases of ankylosing spondylitis are treated every year. Of 195 cases referred for treatment in 1952, 12 had been either misdiagnosed or only belatedly recognized. On going into the reasons for this delay in diagnosis it was found that 12 patients could be divided into four groups, case histories representative of each being given. In the first group pain was not a prominent feature and attention had finally been drawn to the spine by increasing deformity; in the second group a polyarthritis had overshadowed the spinal signs and symptoms; in the third group an industrial accident had been held responsible for symptoms which would otherwise have been investigated more closely; and in the last group the symptoms distributed over various parts of the spinal column, were so mild that they had been ascribed to "muscular rheumatism".

Treatment in such long-standing cases should be both general and local, gold injections and *x*-ray therapy being suggested; breathing and remedial exercises are also advisable. Balneotherapy is regarded as an ideal combination of general and local treatment, but must be continued for many years until the disease process is finally arrested. *D. Preiskel*

500 (*a*). **Corticotrophin Zinc Phosphate and Hydroxide. Long-acting Aqueous Preparations**
J. D. H. HOMAN, G. A. OVERBEEK, J. P. J. NEUTELINGS, C. J. BOOIJ, and J. VAN DER VIES. *Lancet* [*Lancet*] **1**, 541–543, March 13, 1954. 1 fig., 20 refs.

500 (*b*). **Corticotrophin Zinc Phosphate. A Long-acting Aqueous Preparation**
R. GREENE and J. VAUGHAN-MORGAN. *Lancet* [*Lancet*] **1**, 543–545, March 13, 1954. 2 figs., 4 refs.

500 (*c*). **Corticotrophin Zinc Phosphate. A Long-acting Aqueous Preparation**
D. G. FERRIMAN, A. B. ANDERSON, and P. P. TURNER. *Lancet* [*Lancet*] **1**, 545–546, March 13, 1954. 1 fig., 3 refs.

500 (*d*). **Corticotrophin Zinc Phosphate. A Long-acting Aqueous Preparation**
S. A. DEN OUDSTEN, L. VAN LEEUWEN, and R. J. COERS. *Lancet* [*Lancet*] **1**, 547–549, March 13, 1954. 4 figs., 4 refs.

The adsorption of an active drug on to a flocculent precipitate is a standard means of concentrating it and prolonging its period of effective action on injection. This technique has now been applied to corticotrophin (ACTH), since to obtain prolonged action from a single injection would be an advantage both clinically and economically, although concentration is not an important problem. These four papers deal with the adsorption product of corticotrophin and zinc phosphate.

In the experiments reported by Homan *et al.* the combined product was shown to have an effect on the liver glycogen content of hypophysectomized rats greater than that of the same amount of ordinary corticotrophin in aqueous solution given in hourly doses over the same period (8 hours), while the reduction in weight of the thymus was equivalent to that produced by doses of the aqueous solution 10 to 32 times greater. Inactivation of ordinary corticotrophin by serum enzymes *in vitro* was considerable, but protection from enzymatic destruction and good stability was evident in the zinc suspensions in the presence of serum. A solution of 20 units of corticotrophin and 1 to 2 mg. of zinc chloride per ml. at *p*H 3·0 showed excellent stability on storage, and for clinical or biological use it was precipitated with trisodium phosphate and a final *p*H of 6·5 obtained by the addition of sodium hydroxide. Precipitation immediately before clinical use prevented crystallization in the flocculent suspension.

The effect of the combination of corticotrophin with zinc phosphate was compared with that of aqueous corticotrophin in 6 cases of rheumatoid arthritis by Greene and Vaughan-Morgan, the degree of amelioration of symptoms and increase in the urinary excretion of 17-ketosteroids (total neutral fraction) produced by each preparation being assessed. The effect of the combination on the symptoms was, in all but one case, better than that of ordinary corticotrophin, and was more lasting in 4 cases, the lack of superiority of the zinc preparation in the other 2 cases being attributed to an unusually prolonged effect of ordinary corticotrophin. The symptomatic effect of each injection of 20 units of

the combination lasted 2 days or more, but better results were obtained by giving daily injections of 10 to 20 units. The 17-ketosteroid output was usually more than double that produced by ordinary corticotrophin in a similar dosage.

Ferriman *et al.* compared the clinical effects of the corticotrophin–zinc-phosphate preparation and an "ethyl-oleate–beeswax preparation of corticotrophin" in 7 cases of rheumatoid arthritis and one of ankylosing spondylitis. The latter preparation was never effective for more than 24 hours, whereas the effect of the former lasted 24 to 48 hours. Treatment with the zinc phosphate preparation resulted in a constant and persistent decrease in the eosinophil count and an increase in 17-ketosteroid excretion, whereas the effect of the ethyl oleate preparation was variable, although more constant than with ordinary corticotrophin.

Corticotrophin zinc phosphate was used by den Oudsten *et al.* in 25 cases of rheumatoid arthritis. Although the therapeutic effect did not differ essentially from that obtained by frequent injections of ordinary corticotrophin, they point out that "corticotrophin zinc phosphate stimulates the adrenal gland for 24 to 48 hours or more after a single injection, as reflected by the eosinophil response and the urinary excretion of 17-ketosteroids, sodium, and potassium. A single injection of 20 I.U. of corticotrophin zinc phosphate has the same effect as 4 doses of 20 I.U. of ordinary corticotrophin injected 4-hourly". The action of zinc phosphate corticotrophin on the eosinophil count was found to set in as quickly as that of ordinary corticotrophin, but did not reach a maximum until about 8 hours after the injection and was much more prolonged. *Harry Coke*

501. **Use of Phenylbutazone in Rheumatoid Arthritis**
M. PEMBERTON. *British Medical Journal* [*Brit. med. J.*] **1**, 490–493, Feb. 27, 1954. 12 refs.

Phenylbutazone was tried at Withington Hospital, Manchester, in the treatment of 186 patients with chronic polyarthritis of the rheumatoid type and 24 with degenerative hip disease. During the investigation, which did not include a control series of cases, other forms of treatment, including gold injections, were continued. In assessing the results the effect of rest in bed was discounted. The average dose of phenylbutazone was 600 mg. daily. Patients were examined before, and 3 and 6 months after, beginning treatment. Subjective improvement was judged by the patient's capacity for, and comfort during, normal activity.

After 3 months' treatment the condition of 156 patients was reviewed. It was found that the drug was of "little or no value" in 36, of "moderate value" in 104, and of "considerable benefit" in 16. The erythrocyte sedimentation rate was apparently not affected. Toxic reactions occurred in 92 cases, about 25% of all patients having to cease treatment on this account. Reactions included gastrointestinal symptoms, including gastric haemorrhage, rash, oedema, fever, soreness of the mouth, and a few, infrequent, manifestations of doubtful origin. There was no correlation between the serum level of phenylbutazone and the incidence of toxic reactions.
G. Loew

502. **Injectable Phenylbutazone in Rheumatism.** (La phénylbutazone injectable en rhumatologie)
S. DE SÈZE and J. LEVERNIEUX. *Presse médicale* [*Presse méd.*] **62**, 203–205, Feb. 10, 1954.

The authors report their results in 700 cases of rheumatism which, since January, 1952, they have treated with phenylbutazone given parenterally. The conditions for which the drug was administered included gout, rheumatoid arthritis and spondyloarthritis, tendinitis and tendino-bursitis, arthroses, and radiculalgia. The general plan of treatment was to begin with a course of intravenous infusions of 1 g. of phenylbutazone in a 10% solution given daily or on alternate days. As symptoms subsided, usually in the second week of treatment, intramuscular injections of a similar dose of phenylbutazone, with triethylene glycol and procaine, were substituted for the infusions, and these were also given daily or on alternate days. Subsequently the intervals between injections were gradually increased, until for chronic cases individual maintenance doses were established.

The best results were observed in cases of gout and ankylosing spondylitis. In cases of rheumatoid arthritis they were inconstant. With adequate dosage, the maximum effect of the drug was observed from the beginning of treatment. The authors regard the following three precautions as indispensable: (1) the patients should be carefully selected, cachectic cases and those having an abnormal blood picture or a history of gastric and cardio-renal disease being excluded; (2) during treatment a strict sodium-free diet must be enforced; (3) treatment should be suspended at the first sign of complications, such as digestive disturbances, peripheral oedema, haemorrhage, or cutaneous eruptions. *A. Swan*

503. **Stigmonene Bromide in the Treatment of Muscular Spasm**
H. F. MULHOLLAND and J. H. O'CONNELL. *Journal Lancet* [*J.-Lancet*] **74**, 90–94, March, 1954. 2 figs., 20 refs.

"Stigmonene" bromide is a synthetic, alkaloid-like salt of the quaternary pyridinium series having a slightly less powerful cholinergic action than neostigmine but the advantage of being of lower toxicity. This drug was given parenterally in doses of 0·5 to 4 mg. twice weekly to 64 out-patients attending St. Vincent's Hospital, New York, for the treatment of muscular spasm associated with osteoarthritis, rheumatoid arthritis, and allied conditions.

Increased range of joint movement and decrease of pain was obtained in 30 (53%) of 55 patients followed up, and this improvement was maintained in 11 (61%) of 18 treated during the following 10 weeks with saline injections as a placebo. Side-effects, which were minimal and were relieved by oral administration of atropine, included abdominal distress, paraesthesiae, muscular weakness, aggravation of the arthritis (2 cases), and syncope (1 case, doubtfully attributable to the stigmonene). It is emphasized that these cases were far advanced and unlikely to respond dramatically to any form of therapy. The optimum dose of the drug was considered to be 3 or 4 mg. twice weekly. *I. Ansell*

Neurology and Neurosurgery

504. **Amyotrophic Familial Spastic Paraplegia**
S. REFSUM and S. A. SKILLICORN. *Neurology* [*Neuology*] **4**, 40–47, Jan., 1954. 4 figs., 29 refs.

The authors report 3 cases of amyotrophic familial spastic paraplegia which occurred in 3 out of 8 siblings; the 2 surviving patients were fully examined at the University of California School of Medicine, San Francisco, and are here described. The disease, probably due to a recessive gene, began in early childhood as a slowly progressive spastic paresis affecting first the legs, later the arms, and finally the tongue, pharynx, vocal cords, and palate. Extensive muscular wasting, with fasciculation and without evidence of dystrophy, appeared in adolescence. Intelligence was normal, there was no nystagmus or ataxia, and sensation was unimpared; in both the cases examined there was gross scoliosis.

Apart from this last feature and the time of onset and speed of development, the condition at the time of examination was similar to amyotrophic lateral sclerosis. Although in some other reported cases of familial spastic paralysis there has been associated amyotrophy, there were nearly always additional neurological abnormalities, such as ataxia, nystagmus, macular degeneration, optic atrophy, or mental changes, or the onset has been at a later age; furthermore, scoliosis is rare in ordinary familial spastic paraplegia, whereas in the authors' cases it caused gross deformity. *J. Foley*

505. **The Diagnosis of the Congenital Cerebellar Syndrome in Infancy.** (Zur Diagnose des konnatalen Kleinhirnsyndroms beim Säugling)
W. BRENNER and M. HAGEDORN. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **74**, 209–231, 1954. 18 figs., bibliography.

The authors describe the clinical syndrome to be found in infants with congenital malformations of the cerebellum on the basis of a series of 8 cases examined at the University Paediatric Clinic, Bonn, in which pneumoencephalography had confirmed the presence of such a malformation. Certain features were constantly present, while others were variable. The constant features were: (1) marked hypotonia of certain muscle groups—especially of the head and neck, so that the infant could not hold its head up at the usual age; (2) increased tone in the lower limbs, always symmetrical, and usually with increased tendon reflexes; (3) dysphagia and feeding difficulties, often resulting in marasmus, due to incoordination of the bulbar musculature rather than to paralysis; (4) hyperkinesia and movements of the limbs, sometimes resembling choreoathetosis but due to asynergia; and (5) a certain degree of mental backwardness. Less constant features were: (1) episodic vomiting; (2) tonic and myoclonic attacks; (3) incoordination of the eye movements, withbut nystagmus; and (4) definite thickening of the cranial vault over the occipital protuberance and ridge.

The diagnosis of the malformation during life rests on the pneumoencephalogram, the appearances being of three types, depending on the type of deformity of the cisterna magna. The clinical picture may vary as the child grows, new signs appearing and others being modified. The aetiology and differential diagnosis of the condition are discussed. *J. B. Stanton*

506. **The Treatment of Dystrophia Myotonica with A.C.T.H.**
O. GARAI. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 83–86, Feb., 1954. 5 refs.

The author describes the results obtained at King's College Hospital, London, with ACTH in the treatment of 4 patients suffering from dystrophia myotonica. The myotonia was somewhat relieved, but in those cases in which wasting and dystrophy of the muscles were prominent features ACTH had little noticeable effect. This drug was preferred to cortisone because in previously reported cases the latter had proved of little value. The possible mode of action of ACTH on myotonia is discussed in relation to its effect on the potassium content of muscle. *J. B. Stanton*

507. **Tourniquet Paralysis Syndrome**
J. MOLDAVER. *Archives of Surgery* [*Arch. Surg. (Chicago)*] **68**, 136–144, Feb., 1954. 2 figs., 12 refs.

This paper is based on the study of 7 cases of complete tourniquet paralysis, of which 2 are described in detail as characteristic of the group. The author considers that the disturbance of function in peripheral nerves following prolonged application of a tourniquet results from mechanical pressure and not from ischaemia. The syndrome of tourniquet paralysis has not been clearly defined in the past: there is paralysis, with diminished muscle tone but with no subsequent muscular atrophy; sensory loss is dissociated, touch, pressure, vibration, and position sense usually being lost, whereas pain sensation is never lost and there is often hyperalgesia, while temperature sensation is normal or only slightly disturbed; on releasing the tourniquet there are no paraesthesiae, suggesting that the touch fibres are blocked at the point of pressure. There is no tendency for a neuroma to develop at the site of injury.

Electrical studies show lack of response to stimulation of motor fibres above the injury, but good response below. Stimulation of sensory fibres proximal to the lesion produces tingling, but stimulation below the injury does not, so that electrical stimulation can be used to locate the precise level of damage. The area of damage is narrow and is found at the site of maximum pressure. When the syndrome is complete, recovery may take 3 months or even longer. *Hugh Garland*

BRAIN AND MENINGES

508. **The Pedunculus Cerebri and the Capsula Interna.** [In English]
W. J. C. VERHAART and K. MECHELSE. *Monatsschrift fur Psychiatrie und Neurologie* [*Mschr. Psychiat. Neurol.*] **127**, 65–88, Feb.–March, 1954. 7 figs., bibliography.

The Häggqvist methyl-blue–eosin staining technique provides a means of estimating the relative numbers of nerve fibres of different thickness in fibre tracts. After ablation of different areas of the cerebral cortex in monkeys this method was used by the authors as a means of studying the origin of the fibres in the internal capsule and the cerebral peduncles. The results confirmed much of what is already known. Thus of the 3 areas which can be distinguished in the peduncles and internal capsules, the medial one, corresponding to the fronto-pontine tract in man, derived its fibres from the frontal lobe (part of Area 6 and Areas 8, 9, and 10), and the middle one, corresponding to the pyramidal tract in man, originated mainly in the precentral convolution. Fibres in the lateral area, however, did not originate in the temporal lobe, as is sometimes stated, but in the parieto-temporal gyri. No fibres from the striate area of the occipital lobe could be found in the peduncles. It was found possible in the internal capsule to distinguish thalamo-cortical and cortico-thalamic fibres from the corticofugal fibres descending into the peduncle.

L. Crome

509. **A Study of Eight Surgically Treated Cases of Spontaneous Subcortical Haematoma**
A. WERNER. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 57–69, Feb., 1954. 15 figs., 25 refs.

The clinical features and the surgical treatment of 8 cases of intracerebral haematoma are described in detail in this paper from the University Neurosurgical Clinic, Zürich. Generally the patients were middle-aged, the average age of the 6 men being 39 and the ages of the 2 women being 43 and 52 years respectively. In all the cases there was a prodromal period lasting 2 weeks to a few months, during which the patient complained of headache. The onset of the illness was usually sudden, with severe unilateral headache, vomiting, neck stiffness, increasing drowsiness, and focal signs appropriate to the situation of the haematoma. An important diagnostic feature was the unilateral headache, which in all the cases was related to the side of the haemorrhage. There was usually some spontaneous improvement during the first two weeks following the acute phase. In all the cases subarachnoid haemorrhage occurred.

Angiography revealed an avascular mass in the brain, and the author considers that this finding, when associated with subarachnoid haemorrhage, is diagnostic of an intracerebral haematoma. In half the cases pneumoencephalography disclosed a large intracerebral cavity communicating with the lateral ventricle. Although the electroencephalogram showed focal abnormalities, it was of little help in determining the exact location of the haematoma. Surgical treatment consisted in exposure of the area involved, removal of the haematoma, and careful haemostasis. Of the 8 patients, 6 made a good recovery, one had a serious residual neurological disability, and one died of a pressure cone after operation.

The author stresses the need for surgical removal of the haematoma; he does not consider, however, that burr-hole aspiration or decompression is of any value in treatment. In his view the haemorrhage, the cause of which was not established in any of his cases, is arterial in character, the probable sequence of events being repeated arterial spasm, leading to ischaemia and damage to arterial walls, with subsequent rupture and haemorrhage.

[In spite of the author's contention that no aetiological factor was found, the findings at operation in 3 cases suggest that an angiomatous malformation was responsible for the haemorrhage. Thus in one case he found that " in the bottom of the cavity there was a spherical mass covered with fibrin and containing numerous fine arterial vessels. . . . The excised mass comprised fibroplastic tissue containing much haemosiderin and haematoidin, small and large vessels, but no neoplastic tissue ". In another case he observed that " towards the occipital lobe there was a vascular mass the size of a cherry draining into dilated veins. Subcortically the mass communicated with a huge cavity . . . filled with clotted blood "; while in a third case he found that " after the haematoma had been taken out there remained, dorsal to the temporal horn, a greyish-red mass which was partially excised. . . . The excised discoloured tissue proved to be a granulation tissue with organized haemorrhage ".]

Brodie Hughes

510. **Acquired Epilepsy. A Study of 535 Cases**
B. SMITH, G. C. ROBINSON, and W. G. LENNOX. *Neurology* [*Neurology*] **4**, 19–28, Jan., 1954. 4 figs., 10 refs.

The authors report, from the Children's Medical Center, Boston, a study of 535 patients, most of whom were out-patients, with epilepsy due to organic brain disease. One-third of them were children under the age of 12, and in 90% of all cases the first fit had occurred before the age of 20. There was a family history of epilepsy in 24%. Evidence, or presumptive evidence, of cerebral damage was obtained from the patient's history in 88% and from focal electroencephalographic abnormalities in 75%; a focal aura or onset of the fits, present in 51%, was also regarded as evidence of organic disease; and abnormal neurological signs were found in 50%. In a small group amounting to 12·3%, although there was clinical evidence of brain disease, there was no clue in the history as to its cause or time of onset. Prenatal causes were judged to account for 13·3% of the cases, half being in premature babies. Birth injuries accounted for 30·1%, postnatal injury for 20·7%, infections for 17·2%, and miscellaneous conditions for 6·4%, while in 12·3% the cause of the condition was unknown. Cases in which there had been febrile convulsions followed by signs of organic disease were included in the group attributed to infections.

In about half the cases (46%) fits began within one year of the causative event, in 20% they began within 2 years, while in only 12% did they begin after a lapse of

over 10 years. Epilepsy starting 10 years or more after the suspected injury was encountered most often in the prenatally affected group. A graph, in which the percentage of cases in each causal group was plotted against the age when fits began, showed that birth injury was the most prominent cause in the first half of childhood, while postnatal trauma assumed a steadily greater importance as the second decade was passed [a not very surprising conclusion]. Infections were a fairly steady source of epilepsy throughout the first three decades, and in 72% of such cases the epilepsy began within one year of the infection. In the authors' view, febrile convulsions initiate epilepsy only in childhood. The results are compared with those of a previous survey by one of the authors (Lennox, *New Engl. J. Med.*, 1933, **204**, 386) from which they differ considerably. *J. Foley*

511. **Mesantoin in the Treatment of Epilepsy. A Study of Its Effect on the Leukocyte Count in Seventy-Nine Cases**
J. A. Abbott and R. S. Schwab. *New England Journal of Medicine* [*New Engl. J. Med.*] **250**, 197–199, Feb. 4, 1954. 2 figs., 8 refs.

Leucocyte counts were carried out every week at the Massachusetts General Hospital (Harvard Medical School), Boston, on 79 patients receiving " mesantoin " (methoin) in an average dose of 100 mg. 3 times a day for the treatment of epilepsy. In 18 cases the absolute neutrophil count was at one time or another below 2,500 per c.mm. However, in only 2 of these 18 was the count as low as 1,600 per c.mm., which the authors took to be the critical level, although administration of the drug had to be stopped owing to poor cooperation on the part of the patient in 3 other cases in which the count fell below 2,000 per c.mm. There were no symptoms or signs associated with the leucopenia, and the authors note [as have others] that even frequent leucocyte counts do not provide a complete safeguard against the sudden development of agranulocytosis. The leucocyte count appeared most likely to fall between the 5th and 8th months of treatment. In all cases the count rose promptly after treatment was stopped. *G. S. Crockett*

512. **Post-encephalitic Parkinsonism with Amyotrophy**
J. G. Greenfield and W. B. Matthews. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 50–56, Feb., 1954. 23 refs.

The authors describe 2 cases of postencephalitic Parkinsonism with oculogyric crises in men aged 39 and 57 respectively admitted to King's College Hospital, London. In both cases there was late development of progressive spinal amyotrophy which, in the younger man, finally produced a condition clinically indistinguishable from amyotrophic lateral sclerosis. The older patient became progressively more helpless and died from bulbar paralysis a few days after admission.

A full report is given of the post-mortem findings, which corresponded closely with the clinical picture, in this case. Severe loss of cells in the substantia nigra and locus caeruleus, with degenerative changes in the globus pallidus, could be related to the Parkinsonism. Interesting changes in the oculomotor nucleus, namely, neurofibrillary degeneration, Lewy inclusion bodies, and a senile plaque, may have provided the basis for the oculogyric crises. The relation of the amyotrophy to loss of anterior horn cells in the cord was evident, but no neurofibrillary changes were seen at this level. Large axonal swellings were found in the bases of the dorsal and ventral horns. There was no evidence of tract degenerations. The pathogenesis of this post-encephalitic amyotrophy is discussed. *J. B. Stanton*

513. **Clinical Evaluation of Pagitane Hydrochloride in Parkinsonism**
R. S. Dow and G. N. Smith. *Neurology* [*Neurology*] **4**, 33–39, Jan., 1954. 13 refs.

" Pagitane " (cycrimine hydrochloride), an aminopropanol which has some chemical resemblance to benzhexol, was tried at the University of Oregon Medical School, Portland, in the treatment of 23 patients with Parkinsonism, 7 of whom, although exhibiting tremor, were not true examples of the Parkinsonian syndrome; 10 of the patients had already been treated with " artane " (benzhexol hydrochloride). The initial dose of pagitane was 1·5 mg. 5 times a day, increasing to 25 mg. daily or until side-effects became apparent; these included dryness of the mouth, constipation, blurred vision, mental confusion, dysphagia, and conjunctivitis, and were severe enough in 10 cases to cause withdrawal of the drug.

There was objective improvement in 13 of the 23 cases. The best results were obtained in Parkinson's disease and postencephalitic Parkinsonism; patients in whom tremor was the main symptom and patients with cerebral arteriosclerosis showed no improvement. Thus while pagitane appears to be about as effective as artane, it has the advantage that it can sometimes be given in larger doses. *J. Foley*

514. **Procaine Injection of the Globus Pallidus in Parkinsonism**
I. S. Cooper. *Psychiatric Quarterly* [*Psychiat. Quart.*] **28**, 22–23, 1954. 3 refs.

The author has previously reported (*Psychiat. Quart.*, 1953, **27**, 317) that some of the disability of advanced Parkinsonism—particularly incapacitating rigidity—may be alleviated by ligation of the anterior choroidal artery, which supplies the medial segment of the globus pallidus. After a study of the anatomical relations of the latter structure he has developed a technique whereby procaine and other solutions may be injected into its vicinity by means of a small-calibre ventricular needle introduced through a trephine hole in the skull. In 2 cases of Parkinsonism the injection of 0·5 ml. of 0·5% procaine solution resulted in the immediate disappearance of tremor and rigidity from the contralateral limbs, the effect lasting for more than 24 hours. The effects of injections of other substances are now being studied.

[The author claims that the procedure described " should bring the tip of the ventricular needle into close approximation with the globus pallidus ", but the practical details given are insufficient to enable the validity of this claim to be judged.] *Donald Crowther*

Psychiatry

515. **Pain as an Old Friend**
J. PENMAN. *Lancet* [*Lancet*] **1**, 633–636, March 27, 1954.

In this paper from Hertford County Hospital the author discusses the reactions of patients to the removal of long-standing pain, as illustrated by the results in 275 personal cases successfully treated for tic douloureux by injection of the trigeminal sensory root with alcohol. After severe pain has been present for 6 months or more the individual may develop certain emotional reactions towards it. Thus the pain may become, as it were, his prime, all-excluding occupation, or on the other hand it may act as a stimulus to courage; in others, it may lead to ritual habit formation, such as manœuvres for the avoidance of draughts. In some cases it may act as an alternative to a neurosis by providing a refuge from an intolerable situation, or it may be perpetuated by dominant relations who force the patient into an " invalid situation ".

When the pain is removed, patients in whom emotional forces of this kind are at work suffer a sense of loss, which may lead to grief or depression, to the appearance of further symptoms, or to denial of their improvement and exaggeration of the effects of the accompanying paraesthesiae. The age of the patient and duration of the pain seem to be less important in bringing about these reactions than the basic personality; inactive, dependent persons are more numerous among those who are dissatisfied after their pain is removed. The author stresses that it is the responsibility of the physician not to allow curable pain to become chronic, and that he should personally assess the patient's personality before treatment and, most important, follow up by interview those who are likely to miss their pain and to require support and reassurance afterwards; in some cases, also, explanation to the relatives is required. A number of typical case histories are given, including two which illustrate the beneficial effect of taking up some employment on patients who had not worked for many years.

J. B. Stanton

516. **The Varying Response to Pain in Psychiatric Disorders: a Study in Abnormal Psychology**
K. R. L. HALL and E. STRIDE. *British Journal of Medical Psychology* [*Brit. J. med. Psychol.*] **27**, 48–60, 1954. 4 figs., 29 refs.

The response to pain was investigated in some 270 psychiatric patients admitted to Barrow Hospital, Bristol, and the attached Neurosis Centre and classified as suffering from depression, anxiety, or schizophrenia (those with organic psychoses or epilepsy being excluded). Heat stimulation was applied repeatedly to the forehead for 3 seconds at a time, the intensity, measured on a microammeter scale, being increased by equal steps and the patients' description of, or reaction to, each stimulus being recorded. Three thresholds were defined—the " warmth perception point ", the point of " verbal report of pain ", and the " pain reaction point ", occurring typically in that order. Differences between age groups, between sexes, and between diagnostic groups were investigated, and also the effects of electric convulsion therapy and of leucotomy.

The results varied over a wide range in each group, but in general the depressive and schizophrenic patients tended to be more tolerant of pain than the anxiety neurotics. Increase in age increased the threshold for both perception of and reaction to pain in the neurotic and depressive patients, whereas that for perception of warmth was unaffected. In depressive patients who improved clinically after convulsion therapy there was also a highly significant reduction in the pain thresholds, in contrast to a comparable group who were untreated or not improved. The authors' main conclusion is that the variation in pain tolerance thus measured within the population examined could be attributed to differences in central attitude and not to differences in peripheral sensitivity. These differences are discussed in terms of learning mechanisms and of constitutional factors, but it is pointed out that too little is known about normal variation for such findings to be of value in the understanding of the mechanisms of the different forms of personality disturbance.

N. A. Standen

517. **Psychophysiological Investigations in Experimental Psychoses: Results of the Exhibition of D-Lysergic Acid Diethylamide to Psychiatric Patients**
B. SLOANE and J. W. L. DOUST. *Journal of Mental Science* [*J. ment. Sci.*] **100**, 129–144, Jan., 1954. 39 refs.

D-Lysergic acid diethylamide, a derivative of ergot, was discovered a few years ago to produce psychosis-like symptoms when given in minute doses to mentally normal subjects. In a study carried out at the Maudsley Hospital, London, the authors administered 40 μg. of this substance to 14 healthy control subjects, 7 schizophrenic patients, and 12 patients with depression. Psychological observations confirmed the earlier findings, reported by a number of workers, except that the changes in mood provoked by the drug were not all of the cheerful and euphoric kind, but depended largely on the original affective state of the subject. The results of psychological tests measuring various types of function showed no significant deterioration. Physiological changes under the influence of the drug were studied mainly by the oximetric methods developed by Doust. Spectrometric oximetry was carried out during pain tests and under other forms of mental stress. While the control subjects and depressed patients showed results indicative of increased autonomic lability, the schizophrenic patients proved refractory and were hardly affected [as one would expect]. The authors point out [and the abstracter agrees] that more sensitive physiological tests and recording methods are needed in the study of experimental intoxications of this kind in human beings.

[On the whole, the study described should be regarded as of the nature of a pilot investigation which should lead to further detailed and more fruitful studies. The attack on the problem as described in the present article was directed to too many points at once and in too few experiments to yield any important results.]

W. Mayer-Gross

518. **The Pathophysiological Mechanisms of Hypochondriacal Hallucinations.** (О патофизиологических механизмах ипохондрического бреда)

Y. G. KOZLOV. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **53**, 935–941, Dec., 1953. 1 fig., 18 refs.

The author suggests that hypochondriacal hallucinations are based upon impulses from internal organs which are the seat of some local disturbance, and that if this theory is correct, then the interruption of these impulses should terminate the condition. He has therefore tried such treatment in the form of a combination of intravenous injection of procaine with sleep therapy. Encouraging results were obtained in the 3 cases described in this paper. He also reports some observations on the effect of the intravenous administration of procaine in cats.

L. Crome

TREATMENT

519. **Effect of Cortisone in Treatment of Psychotic Illnesses**

J. B. COHN, G. A. STECKLER, and J. RUBINSTEIN. *Journal of Clinical and Experimental Psychopathology* [*J. clin. exp. Psychopath.*] **14**, 161–175, Oct.–Dec., 1953. 37 refs.

The effect of cortisone on 21 disturbed, regressed, male psychiatric patients who had failed to respond to other treatment was studied. All but 2 of the patients were schizophrenics. (Treatment of a control group with a placebo was started, but had to be abandoned.) An average dose of 400 mg. of cortisone was given daily for one month in each case. Toxic effects were few, minor, and reversible.

Clinically, 9 patients were improved within one month after finishing treatment, and 6 of the 9 were later discharged (but 4 of the 9 had subsequently had electric convulsion therapy). However, the results of various psychological tests carried out before treatment and during the last week showed little significant change, except for increase in the Rorschach M+ and F+ scores and decrease in the number of Rorschach rejections, which may have been due to the withholding of convulsion therapy. Excretion of 17-ketosteroids increased in the group as a whole, but diminished in the improved cases. ACTH responsivity (Thorn test) was adequate before treatment and diminished after treatment in the whole group. Certain electroencephalographic changes were recorded.

The results of previous studies of adrenocortical function in psychotic illness are reviewed and the present findings discussed critically. The authors conclude that while much additional experimentation is required, the indices of adrenocortical function in current use are unsatisfactory for the purpose of evaluating adrenal function in psychotic patients, and it is recommended that direct methods be developed for the determination of specific blood corticoid levels.

A. C. Tait

520. **Chlorpromazine. New Inhibiting Agent for Psychomotor Excitement and Manic States**

H. E. LEHMANN and G. E. HANRAHAN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **71**, 227–237, Feb., 1954. 10 refs.

At the Verdun Protestant Hospital, Montreal, 71 psychiatric patients aged 18 to 82 were treated with chlorpromazine ("largactil") for periods up to 4 months. A single intramuscular dose of 50 to 100 mg. usually controlled psychomotor excitement in such conditions as manic-depressive psychosis, catatonic schizophrenia, schizo-affective conditions, epileptic clouded states and organic–toxic confusional states, and agitation occurring in lobotomized patients within 24 hours. Emotional tension was generally controlled by an oral dose of 50 to 200 mg. daily, but up to 800 mg. a day was administered in some cases.

Relapses were uncommon, occurring less frequently than after electric convulsion therapy. Chlorpromazine quietens the patient without producing confusion or causing inaccessability, in contrast to other sedatives. It does not cause emotional disinhibition, but selectively inhibits drive. Allergic reactions were observed in 13% of cases and gastrointestinal trouble in 8%.

A pronounced fall in blood pressure was recorded and the pulse rate increased. Mild hyperthermia up to 101° F. (38·3° C.) was usual. In 3 cases jaundice developed, after 2, 3, and 4 weeks' treatment respectively, but cleared rapidly on omitting the drug. Some slight abnormality of liver function was suggested by the cephalin–cholesterol flocculation test in about half the cases.

G. de M. Rudolf

521. **The Effect of 1-*iso*Nicotinyl-2-*iso*propyl Hydrazide (IIH) on the Behavior of Long-term Mental Patients**

G. R. KAMMAN, J. G. FREEMAN, and R. J. LUCERO. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **118**, 391–407, Nov., 1953 (received March, 1954). 19 figs., 2 refs.

It has been reported that 1-*iso*nicotinyl-2-*iso*propyl hydrazide (iproniazid, "marsilid") produces an increased sense of well-being in patients under treatment for tuberculosis. This suggested to the authors of this paper that the drug might have a positive action on the higher centres and might therefore have an effect on the behaviour of long-term mental patients. In a carefully controlled and evaluated experiment carried out at Fergus Falls State Hospital, Minnesota, they studied three groups, each of 30 female patients with chronic psychoses, who were given, respectively, iproniazid, a placebo, and no treatment. The identity of patients receiving iproniazid and placebo tablets was known to the dispensing pharmacist only—at least during the first 8 weeks of the experiment, which extended over 24 weeks. The average behaviour rating, as measured by the L–M

Fergus Falls Rating Scale (Lucero and Meyer, *J. Clin. Psychol.*, 1951, **8**, 250), and body weight of each group were recorded weekly.

Although the differences between the groups were never great enough to be statistically significant, certain trends were observed in the group receiving iproniazid which suggested that the drug had a slight beneficial effect. However, it was found that the " total push " method of treatment without the use of special drugs, carried out on another group of patients at the same hospital, gave far better and more significant results in respect of behaviour. *F. K. Taylor*

522. **Further Studies on Endocrine Treatment in Adolescence and Early Adult Life**
D. E. SANDS. *Journal of Mental Science* [*J. ment. Sci.*] **100**, 211–219, Jan., 1954. 17 refs.

The author describes his clinical experiences with the use of dehydro-*iso*androsterone (" diandrone ") and of oestrogens for the treatment of character abnormalities and personality difficulties in young people at St. Ebba's Hospital, Epsom, Surrey. Diandrone was administered to 57 patients with inadequate personality and evidence of physical immaturity, of whom 38 were male juveniles or adolescents aged between 12 and 20, 6 were females aged between 11 and 37, and 13 were adult men aged 21 to 37. After various periods of treatment they showed increase in self-confidence, activity, improved performance in school or occupation, and a better ability to discuss their feelings in psychotherapeutic sessions. The dosage ranged from 5 to 30 mg. given by mouth. The author considers that this treatment is contra-indicated in aggressive psychopaths and schizophrenics, and in all cases with manic features. Established homosexuality or other established sexual abnormality was little influenced or in some cases increased by treatment, but a mild tendency to homosexuality gave way to heterosexual interests. On the whole, the author concludes, " diandrone exerts an androgenic effect in a social and psychological rather than in the physical sexual field ".

Oestrogens were given to 44 juveniles and young adults who were selected for treatment either because of excessive sexuality or on account of excessive activity in other fields. The dosage varied from 1 to 2 mg. in the first week, with an increase in some cases by 1 mg. weekly to a maximum of 4 to 9 mg. Of 27 patients who were treated for the control of abnormal sex drive, 10 were "markedly improved", 15 "improved", and 2 unchanged. Of 17 cases without sexual difficulties, treated for alleviation of tension and aggression, only 9 showed various degrees of improvement.

[Although such tests, applied without quantitative evaluation of results and without consideration of concomitant factors, can teach us little, the two hormonal substances used in this study seem to have had some psychological influence on the behaviour of psychopathic adolescents. It would be necessary, however, to test these compounds in controlled experiments, excluding as much as possible secondary and subjective factors, before a clear indication of their clinical usefulness can be obtained.] *W. Mayer-Gross*

523. **Further Psychometric Evaluation of the Effect of Mephenesin on Anxiety**
J. H. MENDENHALL and J. A. EWING. *Journal of Mental Science* [*J. ment. Sci.*] **100**, 262–266, Jan., 1954. 10 refs.

An experiment was devised to test the effects of mephenesin on anxiety on 26 alcoholic patients. This was as a follow-up to test the validity of a previous experiment by the authors (in which it was concluded that mephenesin is of little value in alleviating subjective experiences of anxiety). Rigid controls were employed, involving the use of inert tablets for comparison purposes, as well as other safeguards to eliminate subjective factors on the part of the examiner. Using the Behn–Rorschach test–retest as an index of anxiety, it was found that no statistically significant diminution of anxiety was obtained with doses of 2·0 g. mephenesin orally.

It is concluded, from the psychometric data obtained, that mephenesin is of little value in alleviating states of anxiety as measured by the Rorschach and Behn tests. The authors' results in their earlier experiment are corroborated.—[Authors' summary.]

524. **Treatment of Elderly Psychiatric Patients. Use of a Diagnostic Classification**
V. NORRIS and F. POST. *British Medical Journal* [*Brit. med. J.*] **1**, 675–679, March 20, 1954. 5 refs.

Of 192 consecutive patients over 60 years of age attending a psychiatric clinic, 188 could be classified in one of three broad diagnostic groups: (1) dementias of old age —that is, irreversible disorganizations of personality due to degenerative changes in the brain (46 cases); (2) long-standing neurotic, psychotic, or character disorders (33 cases); and (3) recent affective or toxic-confusional reactions (109 cases). In each category a few cases were classed as " atypical " in that they also showed features characteristic of another category. The classification was made after a single examination lasting 45 to 75 minutes, including physical examination, an account of the condition being obtained from a relative or friend as well as from the patient. It is argued that the application of some such diagnostic screening method to aged patients would be helpful in ensuring that the best use is made of the limited facilities available for treatment.

In this series the classification was not used to determine whether or not the patient should receive active psychiatric treatment, either as an out-patient or in hospital, as opposed to simple nursing care either at home under a general practitioner or in an institution, the treatment in each case being decided individually. Nevertheless, 85 out of the 109 patients in Category 3 were recommended for active psychiatric treatment, whereas in Categories 1 and 2 the numbers were 7 out of 46 and 10 out of 33 respectively, indicating a broad correlation between the diagnostic classification and the treatment requirements of the patient.

The outcome of the treatment recommended, assessed at the end of 12 to 18 months, on the whole confirmed the validity of the advice given, particularly in respect of the response of typical cases of acute affective disorders to active psychiatric treatment.

E. H. Johnson

Dermatology

525. **"Incontinentia Pigmenti": Differentiation of Two Different Syndromes under the Same Name.** (A propos de l' "Incontinentia pigmenti", délimitation de deux syndromes différents figurant sous le même terme) A. FRANCESCHETTI and W. JADASSOHN. *Dermatologica* [*Dermatologica* (*Basel*)] **108**, 1–28, Jan., 1954. 4 figs., bibliography.

The authors discuss at length the literature concerning the two types of incontinentia pigmenti—that now commonly designated the Sulzberger–Bloch type, which they call the classic type, and that described by Naegeli. In addition, they had the opportunity of re-examining the patient in whom the condition was first observed by Bloch in 1925 and the family described by Naegeli in 1928, together with some of their descendants. They are of the opinion that the two types of incontinentia pigmenti are entirely separate entities, even though the histological appearances are similar, pointing out that these appearances are by no means specific and detailing the many other differences which, in their opinion, justify this separation. These are most easily tabulated:

	Sulzberger–Bloch Type	Naegeli Type
Distribution of pigment	Linear	Reticular
Onset of disease	At birth or during the first few weeks of life	At about 2 years
Initial inflammatory lesion	Very frequent	Absent
Ocular changes	Very frequent	Absent
Hair changes of pseudopelade type	Frequent	Absent
Dental changes	Frequent	Constant
Interference with sweat mechanism	Not known	Constant
Palmar and plantar keratosis	Not known	Constant
Sex incidence	Almost entirely confined to female	Attacks both sexes; transmitted as dominant

The authors make a plea for more distinctive names for these conditions, but do not offer any suggestions.

[This is a most interesting article and should be read in full.] *H. R. Vickers*

526. **Atrichia with Papular Lesions; a Variant of Congenital Ectodermal Dysplasia.** [In English]
T. J. DAMSTÉ and J. R. PRAKKEN. *Dermatologica* [*Dermatologica* (*Basel*)] **108**, 114–121, Feb., 1954. 8 figs., 12 refs.

Though dysplasia of ectodermal elements is common, a major ectodermal defect or dysplasia of all or most ectodermal appendages is rare. The authors record the cases of 3 patients who showed almost complete atrichia dating from the early months of life, although all were born with normal growth of hair over most of the scalp. In one patient the affection was familial. A feature in all 3 cases was the presence of numerous papular lesions over the face and much of the body, which showed epidermic cyst formation on histological examination and appeared to arise from ill-developed follicles. In one patient there was some impairment of sweating.

John T. Ingram

527. **The Pseudopeladic State.** (L'état pseudo-peladique)
R. DEGOS, R. RABUT, B. DUPERRAT, and R. LECLERCQ. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph.* (*Paris*)] **81**, 5–26, Jan.–Feb., 1954. 9 figs., bibliography.

In this paper from the Hôpital Saint-Louis, Paris, the authors discuss the relationship of pseudopelade (first described by Brocq in 1885) with inflammatory folliculitis, the keratotic folliculoses, lichen planus, lupus erythematosus, and scleroderma. The histological picture in pseudopelade is as follows. In the early stages the epidermis is thinned and flattened and there are lympho-histiocytic dermal infiltrates around the upper two-thirds of the hairs. A dermal sclero-atrophy follows and the adnexa disappear in the following order: first sebaceous glands, then hairs, then sweat glands, and lastly the arrectores pilorum, without there ever being any evidence of inflammation at the level of the hair bulbs.

The authors have studied 100 cases, in 49 of which biopsy specimens were examined. In 39 cases pseudopelade alone was present, and in 61 other lesions, including scleroderma, lichen planus, and lupus erythematosus, were found. They conclude that pseudopelade is not a disease entity, and that it would be wiser to use the expression "pseudopeladic state".

[This is an important paper which should be read in its entirety.] *James Marshall*

528. **Use of Oral Procaine in Control of Pruritus**
L. G. BEINHAUER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **69**, 188–194, Feb., 1954. 11 refs.

The author, in continuation of his previous work with Thomas and Perrin (*Arch. Derm. Syph.* (*Chicago*), 1952, **65**, 39; *Abstracts of World Medicine*, 1952, **12**, 72) on the use of intravenous injections of procaine for the control of pruritus, now reports the results of treatment with procaine hydrochloride given orally with ascorbic acid to 145 patients suffering from various types of pruritic dermatosis at the Western Pennsylvania Hospital, Pittsburgh; 67 of these patients had obtained no relief from other forms of treatment. Patients whose history

indicated procaine sensitivity were excluded from the study; in those included, preliminary skin tests with 1% procaine hydrochloride showed no sensitivity reactions. Side-effects, including headaches, dizziness, nausea, vomiting, and drowsiness, occurred in 12 cases, but disappeared when administration of the drug was discontinued.

The drugs were given in capsules containing 250 mg. of powdered procaine hydrochloride and 150 mg. of granular ascorbic acid, 2 capsules being given immediately, followed by one capsule every third hour over a period of 2 days, then 6 capsules on the third day, and thereafter 4 capsules daily, for a total period of 7 to 14 days in most cases. If no relief was forthcoming within 4 days, success with further treatment was found to be unlikely. Complete relief was obtained by 32 (22·2%) of the patients, and temporary relief by 41 (28%); in 72 cases no relief was afforded. The most effective response was obtained in cases of herpes zoster and burning tongue, and also in cases of urticaria due to penicillin.

[It is not clear from the paper whether treatment with ascorbic acid without procaine had been tried previously and had failed.] *Kate Maunsell*

529. **Observations on the Effect of Cortisone in Acne Vulgaris**
J. W. DIDCOT. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **22**, 243–247, March, 1954. 7 refs.

The results of the administration of 25 mg. of cortisone daily to 17 patients with acne vulgaris over periods of 10 to 28 days at the Carle Memorial Hospital, Urbana, Illinois, are reported. In 12 cases there was no clinical effect; in the remaining 5 there was some improvement which was, however, temporary in 3 cases and of limited duration in the other 2. *John T. Ingram*

530. **Experimental and Clinical Observations on the Treatment of Tuberculosis of the Skin with Isoniazid.** (Experimentelle und klinische Erfahrungen bei der Isonicotinsäurehydrazid-Therapie der Hauttuberkulose)
J. MEYER-ROHN and K. H. SCHULZ. *Archiv. für Dermatologie und Syphilis* [*Arch. Derm. Syph. (Berl.)*] **197**, 160–178, 1954. 6 figs., 45 refs.

At the University Clinic of Dermatology in Hamburg-Eppendorf the authors have treated a total of 108 patients suffering from tuberculosis of the skin with 5 to 8 mg. of isoniazid per kg. body weight (up to a maximum of 0·6 g.) a day, given in 4 doses.

Of 76 patients with lupus vulgaris, 30 were clinically cured, and 40 improved. The degree of improvement obtained was related to the duration of treatment, which was over 8 months in most of the cases in which the disease was cured. Some of these cases had previously failed to respond to vitamin D_2 and to "conteben" (thiacetazone). However, biopsy and culture of the excised area of skin gave a positive growth of tubercle bacilli, in spite of clinical improvement or apparent cure and of the disappearance of tuberculoid structures, in 13 out of 17 cases after 4 to 5 months' treatment, and prognosis must therefore be guarded.

Of 9 patients with tuberculous cervical lymphadenitis, 4 had an associated tuberculosis cutis colliquativa, and these responded better to isoniazid than those with closed lesions. There were 15 cases of Bazin's erythema induratum or papulo-necrotic tuberculid which, the author considers, were distinctly helped by isoniazid, but in view of the naturally varying course of the tuberculids they refrain from drawing any firm conclusions. Eight cases of tuberculous ulceration of the mucosa of the mouth (associated with open pulmonary disease) healed in a maximum of 8 weeks, with improvement in the patient's general condition and some radiological improvement. The sputum, however, remained positive and the drug was continued for 3 months after healing of the mouth lesions.

Side-effects, which occurred in 14 cases, were chiefly of a minor nature, and only in 3 cases of paraesthesiae had treatment to be discontinued altogether; in the other cases a temporary reduction of dosage or interruption of treatment was sufficient. Routine examinations of the urine, blood, and serum protein level during treatment revealed no abnormality.

A method of culturing tubercle bacilli from biopsy material is described in detail. A special medium is used which is a combination of Hohn's and Dubos's media with the addition of modified Lockemann solution. The sensitivity to isoniazid of tubercle bacilli thus isolated was tested, and urinary isoniazid excretion of 10 healthy control subjects and 5 patients with lupus was assessed. Although the number of assays was small and the excretion of active isoniazid varied within wide limits, the general level of excretion was higher in the patients with lupus than in the control group.
Ferdinand Hillman

531. **Neomycin in Pyogenic Skin Diseases**
R. CHURCH. *British Medical Journal* [*Brit. med. J.*] **1**, 314–315, Feb. 6, 1954. 9 refs.

The topical use of antibiotics for the treatment of pyogenic infection of the skin has been thought by some to have two dangers: (1) the risk of sensitizing the patient and thus preventing future systemic treatment with the antibiotic for a more serious condition; and (2) the encouragement of antibiotic-resistant organisms. As the present author points out, however, neomycin is an antibiotic which has been found unsuitable for parenteral administration and which does not readily give rise to the development of resistant strains of staphylococci. For these reasons it is particularly suitable for the local treatment of common forms of pyodermia.

At the Royal Infirmary, Sheffield, the author has used it with conspicuous success in the treatment of 93 cases of skin infection which included, among others, 48 cases of impetigo, 18 of sycosis barbae, 10 of ecthyma, and 8 of secondarily infected eczema and dermatitis. The antibiotic was applied as an ointment in a strength of 5 mg. per g. of base. This treatment was notably successful in the cases of impetigo and sycosis barbae, and its use is suggested as the first line of attack in these conditions. No sensitization reactions were encountered.
John T. Ingram

Paediatrics

NEONATAL DISORDERS AND PREMATURITY

532. **Chemical Control of Respiration in Newborn Infants**

B. D. GRAHAM and J. L. WILSON. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **87**, 287–297, March, 1954. 2 figs., 13 refs.

In an attempt to evaluate the relative importance of hypoxia, carbon dioxide content, and the *p*H of the blood as stimuli to respiration in the newborn infant, 64 full-term newborn infants were studied at the University of Michigan Medical School. [No mention is made of the method of selection, but presumably only normal babies delivered normally after a normal pregnancy were included.] Capillary blood samples were taken within one hour of birth and once again within 24 hours after birth, and the blood *p*H, the CO_2 content and tension, and oxygen saturation determined by standard techniques.

In almost all the infants there was a definite rise in the *p*H of the blood after birth. The plasma CO_2 content remained unchanged, but the plasma CO_2 tension showed a decisive fall, whereas the blood oxygen saturation rose significantly in the hours after birth. The individual results, which varied very considerably, were grouped according to the amount and type of analgesia or anaesthesia given to the mother during labour, but no significant differences were found. From their findings the authors conclude that oxygen lack plays a considerable, perhaps the main, part in the total stimulus to respiration, and that its site of action is the carotid and aortic bodies rather than the respiratory centre.

David Morris

533. **Haemoglobin Levels in Premature Infants**

M. ARTHURTON, D. O'BRIEN, and T. MANN. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **29**, 38–43, Feb., 1954. 3 figs., 16 refs.

At the Institutes of Obstetrics and Child Health, Hammersmith Hospital, London, the authors investigated the trend of haemoglobin concentration during the first 3 months of life in 22 healthy premature and 17 healthy full-term infants. Details are given of the method employed and the steps taken to avoid possible sources of error, the authors stressing the importance of (1) accurate haemoglobin determination, (2) the use of venous rather than capillary blood for the estimation, and (3) the time when the cord is clamped, since it has been shown that the newborn child at term may be deprived of about 100 ml. of blood if the cord is tied at the moment of birth.

The results of the estimations are given in charts and tables. Consideration of the individual changes in haemoglobin level showed that when the initial value was greater than 20 g. per 100 ml. it tended to fall by more than 10 g. per 100 ml., whereas when the initial level was lower the fall tended to be less. The average rate of decline of haemoglobin level was shown to be greatest between the 2nd and 5th weeks. Although on the average the level reached its lowest point of 10.1 g. per 100 ml. on the 76th day of life, there was considerable variation in the time at which the lowest value was recorded in individual children.

A comparison of the haemoglobin levels in babies of birth weight above and below $3\frac{1}{2}$ lb. (1,580 g.) showed that although the smaller infants tended to reach a lower haemoglobin level than the larger infants between the 8th and 12th weeks of life, the individual values in the two groups varied widely in each 10-day period and the difference was not so striking as had been expected. When the average haemoglobin values for premature and full-term infants were compared, that for the premature group during the first 2 weeks of life was found to exceed that for the full-term group by approximately 1·0 g. per 100 ml., but after the 6th week the position was reversed, the average level in the full-term babies being now between 1·0 and 2·0 g. per 100 ml. higher.

In the authors' opinion these findings suggest that blood transfusion has little place in the care of healthy premature infants. This is in line with their own experience in the Premature Baby Unit of the hospital, where blood transfusions are not normally given to such infants. On discharge each child is prescribed an iron mixture and its general condition checked periodically until the age of 12 months. Iron-deficiency anaemia has not been a problem when this routine was followed.

B. S. P. Gurney

534. **Clinical, Pathological, and Bacteriological Research into Neonatal Mortality.** (Recherches cliniques, anatomo-pathologiques et bactériologiques sur la mortalité néonatale)

P. ROHMER, R. SACREZ, —. HEUMANN, L. FRUHLING, J. LAIGRET, and R. MINCK. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **11**, 1–46, 1954. Bibliography.

The authors review at some length the literature on neonatal mortality, discuss the causal factors, both endogenous and exogenous, and report the results of a detailed investigation of 76 infants, of whom 51 were premature, who died within 30 days of birth at the Clinique Infantile, University of Strasbourg. The infants were examined clinically, bacteriologically, and histologically, necropsy being performed in every case within 3 hours of death.

The adverse influence of prematurity was apparent throughout the neonatal period, becoming less as duration of life increased. Of the premature infants, 37 died within the first 3 days of life, but only one death could be

ascribed to prematurity *per se*. The chief cause of death on the first day of life (23 out of 26 cases) was anoxia associated with cerebral congestion and haemorrhage, a condition distinguished histologically from terminal asphyxia. In 44 cases death was due to infection (in 35 occurring later than the 3rd day), in 2 to malformations incompatible with life, in 1 to blood disease, and in 2 to a " genetic factor ".

Bronchopneumonia of both bronchogenic and haematogenous origin occurred in 42 cases, but it was impossible to say from microscopical examination when or how infection arose, whether following aspiration of amniotic fluid due to uterine anoxia, while in transit through the birth passages, immediately after birth, or later. There were 5 cases of umbilical infection, 1 with suppurating peritonitis, and 4 of meningitis.

The organisms found were mostly *Bacterium coli*, *Proteus*, *Pseudomonas aeruginosa*, and *Streptococcus faecalis*, which were demonstrable in the throat, lungs, bowel, the blood, and other organs. The effects of toxic infection on the liver and on the adrenal cortex were contributory causes of death. It would appear that when its vitality is reduced by maternal illness, Caesarean section, long and difficult labour, injury, or immaturity, the newborn child provides a suitable soil for the development of pathological conditions. It is suggested that treatment of the mother with antibiotics, starting before or early in labour, would greatly reduce neonatal mortality. *V. Reade*

INFANT FEEDING

535. **A Clinical Study of the Draught Reflex in Human Lactation**

C. ISBISTER. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **29**, 66–72, Feb., 1954. 28 refs.

From the Royal North Shore Hospital, Sydney, the author reports the results of her observations made to determine the normal pattern of the draught or " let-down " reflex in human lactation, and the effect of disturbance of it on the suckling infant. The reflex has been shown to be due to afferent impulses from the teat to the posterior pituitary gland causing release of the oxytocic principle, which in turn, it is thought, causes contraction of the myoepithelial cells surrounding the alveoli. Waller (*Brit. J. Nutr.*, 1952, **6**, 210) has also shown that the draught homogenizes the milk. The reflex is inhibited by fear, pain, anger, embarrassment, and injection of adrenaline and can be stimulated by injection of posterior pituitary hormone.

The reflex was investigated in four different ways. (1) Subjective sensation of the mother. This is variously described as a feeling of tingling or " pins and needles " which begins sharply, usually at the start of the feed, and gradually decreases in intensity. Although difficult to describe, it is readily recognized by the mother. (2) Evidence of intermittent leaking or rapid flow of milk from the breast. This was observed to coincide with the subjective sensation. (3) Observation of the sucking movements of the baby at the breast. When the draught reflex has come into action the baby sucks and swallows rhythmically unless the flow is so rapid that the infant is unable to manage it. (4) By the use of the electric breast pump or manual expression to simulate suckling it was shown that suction may have to be applied for 30 seconds or more before the milk flows from the first breast, which can then be emptied in a few minutes. The other breast can be emptied at once without waiting as the milk is already there.

The symptoms associated with disturbances of the reflex are then discussed. A strong draught reflex gives a copious flow of milk, often ejected at high pressure. This may give rise to wind, colic, vomiting, and frequent stools in the infant and sometimes to " fighting " at the breast. In the author's experience the simple manœuvre of " bringing in the milk " by stimulating the nipples before the baby is put to the breast has helped to prevent the development of colic in many infants.

B. S. P. Gurney

CLINICAL PAEDIATRICS

536. **Observations on the Skeletal Age in Mongolism.** (Osservazioni sull' età scheletrica nel mongolismo)

P. MENGHI. *Minerva pediatrica* [*Minerva pediat. (Torino)*] **6**, 81–83, Feb. 15, 1954. 11 refs.

There have been relatively few reports published on the skeletal age of mental defectives as an index of physical development. The present preliminary communication is concerned with a study, carried out at the Paediatric Clinic of the University of Milan, of 16 mongols between the ages of 3 and 14, in whom measurements of height and weight and radiographs of the left carpus were used in computing the expected age. All but 3 patients showed some retardation of growth as judged from both indices, but there was little correlation between the two in the degree of that retardation. It is well known, however, that there are wide variations in normal bone development, and if this is taken into account, only 7 of the present series could be said to fall outside normal limits. Delay in bone growth appeared to be more common in male than in female mongols, but there was no evidence that arrested development was more frequent among older children. *A. Paton*

537. **Birth Weights of Children with Cerebral Palsy**

B. CHILDS and P. R. EVANS. *Lancet* [*Lancet*] **1**, 642–645, March 27, 1954. 3 figs., 5 refs.

The relation of the birth weight of children with cerebral palsy to survival, intelligence, and type of palsy was investigated, 164 such children being divided into four groups: (1) spastic diplegia—48; (2) spastic paraplegia—28; (3) athetosis—52; and (4) hemiplegia—36. Cases of mixed motor disorder were omitted, as also was any case where there was doubt as to the diagnosis, or in which the aetiology was obvious. The intelligence of each patient was assessed from the point of view of whether or not the child was educable, and the birth weight was provided by the mother. The distribution of birth weights in each group was compared with the

normal distribution as given by Karn *et al.* (*Ann. Eugen. (Camb.)*, 1951, **15**, 306, and **16**, 147) among 13,116 infants who survived more than 28 days out of a total of 13,730 born in one hospital over a period of 12 years.

The distribution curves for Groups 1 and 2 were bimodal, but the majority of the children in Group 1 were within the normal weight range at birth, whereas the majority of those in Group 2 were below normal. The former were more likely to be defective in intelligence than the latter, but this was also true of large babies as opposed to small, regardless of the diagnosis. The variance of the distribution of birth weights in the paraplegics was about 3 times the normal, and in the diplegics 5 times the normal. In Group 3 the variance in distribution was also greater than normal, the wide dispersion in these groups suggesting aetiological heterogeneity. In Group 4, however, the distribution did not differ much from the normal in mean or variance. In all four groups it was found that there was a deficiency of infants whose birth weight fell within the range 7·5 to 8·49 lb. (3·4 to 3·85 kg.). Karn *et al.* showed that in their series the optimum weight for survival was 7·97 lb. (3·6 kg.), the lowest mortality being in the 7·5 to 8·49 lb. group.

It is therefore concluded that babies weighing approximately 8 lb. (3·62 kg.) at birth, beside having a better chance of survival, are less likely to have spastic paraplegia or diplegia, athetoid cerebral palsy, or congenital hemiplegia than heavier or lighter infants.

Elaine M. Osborne

538. **Tonsillectomy and Adenoidectomy. A Re-evalution of Results**

J. A. JOHNSTON and T. W. WATKINS. *Journal of Pediatrics* [*J. Pediat.*] **44**, 127–133, Feb., 1954. 2 figs., 21 refs.

Tonsils and adenoids are removed less frequently today than they were 30 years ago, yet few procedures, in the authors' view, have more gratifying results when strict indications are observed. They have assessed the effect of tonsillectomy in a total of 598 children aged 1 to 14 years, the follow-up period being 9 years in 503 and 2 years in 95. The effect of the operation on the incidence of respiratory infections was not easy to assess because this normally declines with the passage of time. Infections of the ear improved and patients with impaired hearing benefited. Abdominal pain for which no cause could be found other than chronic throat infection was relieved by the operation. The incidence of bronchitis became less after tonsillectomy, but this, in any case, tends to decrease with age. Improvement was noted in only half of the patients with sinus infection, the authors observing that in some published reports sinus infection is stated to be more common in patients who have had tonsils and adenoids removed than in those who have not. In asthma the results were generally unsatisfactory, although the authors noted an occasional success in the older child whose nutritional state was impaired and the tonsillar infection always preceded an asthmatic attack. Anorexia improved in 120 out of 144 cases, and in patients suffering from recurrent vomiting there was a reduction in the number and severity of the attacks. The incidence of acute haemorrhagic nephritis and the course of the subacute and chronic forms of the disease were not influenced. Tonsillectomy was followed by improvement in cases of infective arthritis.

From this review of several conditions thought to be influenced by tonsillectomy and adenoidectomy the authors conclude that these procedures are highly beneficial in properly selected cases. *W. Mestitz*

539. **Observations on 73 Cases of Hyperplasia of the Thymus.** (Osservazioni su 73 casi di iperplasia timica) P. MENGHI and P. BRUSA. *Minerva pediatrica* [*Minerva pediat. (Torino)*] **6**, 84–85, Feb. 15, 1954. 15 refs.

There is some disagreement as to what constitutes radiological evidence of thymic enlargement in young infants; on the other hand symptoms suggesting hypertrophy are not always supported by radiography. In 6 years the authors have seen 73 infants at the Paediatric Clinic of the University of Milan whose thymus they considered to be enlarged. All except one were under 2 years of age, the majority being in the first 6 months of life; males predominated. There were no symptoms in 20 cases, the thymic shadow being found on routine radiography for chest infections, and it is questionable whether these can be regarded as examples of thymic hyperplasia. In the remainder the most important symptoms were crises of cyanosis and dyspnoea which occurred during and after meals. Convulsions, cough, and vomiting were less common, and inspiratory stridor was seen on one occasion only. In 44 cases the infant was given *x*-ray therapy in doses of 50 to 100 r, repeated if necessary, with excellent results. Treatment with ACTH in an additional 7 cases was disappointing. Two infants died soon after admission, which emphasizes the need for urgent relief of symptoms. *A. Paton*

540. **Constitutional Stigmata in Asthmatic Children.** (De constitutionele stigmata bij het asthma van kinderen) G. J. HUËT. *Maandschrift voor kindergeneeskunde* [*Maandschr. Kindergeneesk.*] **22**, 73–84, March, 1954. 1 fig.

A study of the clinical records of 187 cases of asthma in children observed for periods of 6 to 19 months showed that 82 of the patients, who suffered considerable incapacitation when in their normal surroundings, nevertheless failed to develop attacks when admitted to hospital (mild cases), whereas in the remaining 105 cases the frequency and severity of attacks was unchanged (severe cases). A correlation was found between the frequency of attacks, the physical signs, and the pattern of respiratory function, which may be ascribed to the dependence of all three on the degree of narrowing of the bronchioli caused by eosinophilic infiltration of the mucosa. Analysis of the clinical features of the mild and severe types indicated that in the latter the family history is more often positive, the incidence of skin affections greater, and the onset earlier by more than a year. The differentiation of the two types is of practical importance in the organization of preventive measures, in prognosis, and in the search for pathogenetic factors.

R. Crawford

541. **The Epidemiology and Incubation Period of Interstitial Pneumonia in Early Childhood.** (Zur Epidemiologie und Inkubation der frühkindlichen interstitiellen Pneumonie)
K. D. BACHMANN. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **74**, 133–140, 1954. 1 fig., 17 refs.

The author discusses the epidemiology and incubation period of interstitial pneumonia with reference to 34 cases in young infants, 15 of whom were premature, seen at Cologne University Paediatric Clinic. In 19 cases the patient had been in hospital previously, and assuming the infection to have been acquired on that occasion, the author estimates the incubation period of the disease to be 40 to 50 days.

In a discussion of means of avoiding infection, the need for standard precautions against cross-infection in hospital is emphasized, particularly as in one case the patient had been exposed to such infection for only 24 hours. The fact that in some cases the disease occurred in the first few days of life leads the author to a discussion of the possibility that it is the result of intra-uterine infection, while the part played by *Pneumocystis carinii*, either as the cause of the condition or as a secondary invader, is also considered. *I. A. B. Cathie*

542. **Salmonellosis in Children**
E. F. RABE. *Pediatrics* [*Pediatrics*] **13**, 247–256, March, 1954. 11 refs.

The author describes 12 sporadic cases of *Salmonella* infection in children between 6 weeks and 12 years of age which occurred in a Pennsylvania town during a period of 18 months. In 3 cases of infection with *S. typhi*, 1 with *S. paratyphi* B, and 3 with *S. choleraesuis* which presented as septicaemia, the organism was recovered from the blood, but not from anal swabs or urine; in 3 cases of infection with *S. typhimurium* and 1 with *S. montevideo* which presented as enteritis the organism was recovered from anal swabs, but not from the blood or urine; while in a case of infection with *S. bareilly* which presented as a pyelonephritis the organism was recovered from an anal swab and the urine, but not from the blood.

The author discusses at length the laboratory methods used in diagnosis and points out the limitations of agglutination reactions. He also outlines the chemotherapy employed. Chloramphenicol proved the most effective agent in controlling the acute phase of the disease, but no drug was consistently effective in removing the organism from the stools of convalescents.
T. A. A. Hunter

543. **The Use of Sulphonamides in the Control of Sonne Dysentery in Day and Residential Nurseries**
A. I. ROSS. *Medical Officer* [*Med. Offr*] **91**, 95–98, Feb. 26, 1954. 1 fig., 12 refs.

The author gives details of 8 outbreaks of dysentery due to *Shigella sonnei* in 7 nurseries during two epidemics in Leicester in the years 1950–1 and 1952–3, with an account of the attempted chemoprophylaxis. The outbreaks occurred in 5 day nurseries for children under the age of 5, the number in each varying from 36 to 47, with a staff of 12 to 18, and in 2 residential nurseries for children under the age of 2. The prophylactic programme was as follows. If 2 loose stools occurred which could not otherwise be accounted for, 3 samples were sent for bacteriological examination; if these were positive for *Sh. sonnei*, other excretors were sought among the remaining children, the staff, and home contacts. All those affected and carriers, if remaining in the nursery, were treated with phthalylsulphathiazole, and this was also given prophylactically to the remaining children and staff. In all cases the dosage was 1 g. for adults, 0·5 g. for children aged 1 to 5 years, and 0·25 g. for children under 1 year, given 3 times a day for 5 days. The stools were retested 2 or 3 days after treatment ceased.

During the first epidemic the above routine was carried out with good results in the 2 day nurseries and one residential nursery affected. In the second epidemic, however, in 2 nurseries the infection was widespread, with many home contacts, and prophylactic treatment, even when the course was extended to 10 days, was of no avail. The infection persisted and spread, and ceased only when treatment was stopped and the remaining cases were sent to hospital. In 2 other nurseries a trial was made of treating only positive carriers. This was less successful, however, fresh cases arising being more severe than the initial ones, and universal treatment was resumed, again with removal of the residual cases to hospital.

Seven strains of *Sh. sonnei* isolated in the second Leicester epidemic were found to be resistant to sulphonamides, including phthalylsulphathiazole, in a concentration of 10 mg. per 100 ml. The author considers that if the number of cases is small it is better to send patients to hospital from a residential nursery, or to exclude them from a day nursery. When the outbreak is widespread chemoprophylaxis is worth trying, since children and staff should be retained in the nursery to prevent further spread. *V. Reade*

544. **Incarcerated and Strangulated Inguinal Hernia in the First Year of Life. Report on 45 Cases**
J. RENDLE-SHORT and C. HAVARD. *British Medical Journal* [*Brit. med. J.*] **1**, 680–682, March 20, 1954. 1 fig., 4 refs.

The authors accept the definition of incarcerated hernia as an irreducible hernia in which there is obstruction to the passage of the contents of the bowel, and of strangulated hernia as one in which the blood supply is also occluded. In a young infant the former may be as dangerous as the latter, and was responsible for 2 of 5 deaths in the series of 45 cases here reported from the United Cardiff Hospitals (Welsh National School of Medicine). The reported incidence of " strangulation " has varied widely owing to differences in interpretation of the meaning of the word by various authors. Inguinal hernia is 9 times more common in male than in female infants, while strangulation, in most cases on the right side, occurred in 25 male and only one female child in a large series reported by Thorndike and Ferguson (*Amer. J. Surg.*, 1938, **39**, 429).

Strangulation in babies is commonest under 3 months of age. In the authors' series, 44 out of the 45 cases of incarcerated inguinal hernia occurred in males, and 42 of these were right-sided. In 16 cases the hernia was irreducible but there were no obstructive symptoms and all the patients recovered. In 29 cases intestinal obstruction was the main symptom, and 5 of these infants died after operation. Clinical details of the 5 fatal cases are given. The authors conclude that strangulated hernia is probably the commonest cause of intestinal obstruction in infants less than 3 months old—excluding congenital obstruction in the first week of life. They emphasize that inguinal hernia in an infant is small and easily missed, being often concealed by the inguinal fold of fat, and therefore in every case of acute intestinal obstruction in an infant the inguinal region should be carefully examined.

Charles P. Nicholas

545. **A Plea for the Longer Treatment of Chronic Pyelonephritis in Children**
J. M. STANSFELD and J. K. G. WEBB. *British Medical Journal* [*Brit. med. J.*] **1**, 616–618, March 13, 1954. 4 refs.

While the treatment of acute pyelonephritis in children with sulphonamides is usually successful, that of chronic pyelonephritis has been much less so. In this paper from the Babies' Hospital, Newcastle upon Tyne, the authors make a plea for more prolonged treatment, in support of which they present the results in two comparable groups of cases treated before and after October, 1950, respectively. The first group (12 cases) were given a 5- to 14-day course (average 7 days) of a sulphonamide or antibiotic in full dosage, and if the condition relapsed, which it often did, the course was repeated. The second group (11 cases) were given sulphonamide (sulphadimidine) in full doses for 10 days and then in reduced doses for a period ranging from 10 days to 6 months.

In the second group, 6 of the 11 patients made an uninterrupted recovery without relapse, whereas only 4 out of the 12 in the first group did so; moreover, the average time for recovery in the second group was less than half that in the first group (38·9 and 83·3 days respectively). The authors stress that the duration of symptoms before treatment is begun should determine the length of treatment on reduced dosage—the longer the history, the longer the treatment. They recommend as a general rule 8 weeks' treatment if the history is of less than 2 months' duration and up to 6 months in longer-standing infections. With this regimen it is thought that relapse can be prevented. The "full dosage" of sulphadimidine used was 0·1 g. per lb. (0·22 g. per kg.) body weight per day. [The "reduced dosage" recommended is not stated, but in 2 of the case histories recorded it is given as 0·5 g. twice daily.] The antibiotic used in most cases was chloramphenicol, and the reported dangers of prolonged use of this drug are recalled; in a few cases aureomycin was employed.

The rationale for the prolonged treatment recommended is that there is inevitably some renal damage in all long-standing cases of pyelonephritis. As the kidney must take some time to heal, and while it is incompletely healed it is more liable to infection, the administration of small doses of chemotherapeutic agents is probably enough to protect the damaged tissue from further infection.

Wilfrid Gaisford

546. **Anomalies and Complications of the Urogenital Tract Associated with Congenital Imperforate Anus**
H. M. SPENCE. *Journal of Urology* [*J. Urol. (Baltimore)*] **71**, 453–463, April, 1954. 14 figs., 8 refs.

547. **The Herpes Simplex Virus in Infantile Eczema**
G. I. BARROW. *British Medical Journal* [*Brit. med. J.*] **1**, 482–486, Feb. 27, 1954. 3 figs., 40 refs.

The complication of infantile eczema known as Kaposi's varicelliform eruption has been shown to be caused by infection of the damaged skin with the viruses of herpes simplex or vaccinia, or much more rarely with other viruses. It is suggested that this condition be called "eczema vaccinatum" and "eczema herpeticum" according to the causal agent.

The present author describes 3 cases of infantile eczema, 2 complicated by eczema herpeticum and one by eczema vaccinatum, and from a review of these and the published literature reaches certain conclusions. The two conditions are much more common in children, particularly young infants, than in adults. The clinical diagnosis depends on the sudden appearance of profound toxaemia, high fever, and a pock-like eruption on an eczematous skin. There may be a history of vaccination, herpes simplex, or contact with one or other virus, which first gains entry through the damaged skin, whence it is rapidly disseminated by the blood stream to localize again in eczematous areas of skin, though occasional lesions appear on previously normal skin. The lesions of eczema herpeticum are greater in number, more uniform in size, and more widespread than those of eczema vaccinatum, which are larger, occurring as groups of firm, almost indurated vesicles with marked local inflammatory reaction. The crusts from herpetic vesicles are easily removed whole, whereas those from vaccinial lesions are adherent and leave a bleeding surface when removed. Enlargement of the lymph nodes is more pronounced in eczema herpeticum.

There is as yet no effective specific treatment. The three patients described were treated with penicillin systemically and aureomycin cream locally, and all recovered in spite of being severely ill. Only in one case was there slight residual scarring, and in none was the underlying eczema altered. The prognosis depends on the virulence of the virus, the susceptibility of the host, the nature and extent of previous skin trauma, and the presence or absence of other secondary infections. In most cases, death from eczema vaccinatum has been due to encephalitis or general sepsis.

All the pock viruses are highly infectious, and patients with eczema should be protected from contact with persons with active herpetic and vaccinial lesions and should not themselves be vaccinated. Cases of eczema herpticum and vaccinatum should be isolated, and it is suggested that the diseases should be made notifiable.

Marianna Clark

Medical Genetics

548. **Personality Differences and Neurotic Traits in Normal Twin Schoolchildren. A Study in Psychiatric Genetics**
J. SHIELDS. *Eugenics Review* [*Eugen. Rev.*] **45**, 213–246, Jan., 1954. 1 fig., 46 refs.

Differences of personality between twins, the incidence of minor nervous symptoms and behaviour disorders among them, and differences in this respect between uniovular and binovular twins were studied at the Maudsley Hospital, London, in 62 pairs of twins selected from normal London schoolchildren. There were 36 uniovular pairs (13 male, 23 female) and 26 like-sexed binovular pairs, all between 12 and 15 years of age. Information was obtained from the parents, supplemented by reports from schools and interviews with the twins themselves, about their social and psychological environment, physical health and development, personality similarities and differences, and the presence or absence of psychiatric maladjustment or neurotic traits.

Psychiatric maladjustment " severe " in degree was present in 42 of the 124 children, and " mild " in degree in 25. Of the remainder, 35 showed neurotic traits. The most common disorders were nail-biting (boys and girls), enuresis (boys), and hysterical attention-seeking and display (girls). This incidence is closely comparable to that in the general population of the same age as estimated by various authorities. Both twins belonged to the same psychiatric group in 25 (69%) of the uniovular and in 8 (31%) of the binovular pairs. Among the uniovular pairs there was concordance (both " neurotic " or both " normal ") in 30 (83%) and among the binovular in 17 (65%). Of the uniovular pairs, 13 (36%) were considered to be " completely concordant " in regard to psychiatric characteristics and behaviour, and 12 (33%) " essentially concordant ", the corresponding figures for binovular pairs being *nil* and 3 (12%). The degree of attachment was much closer for uniovular pairs, but psychiatric similarity was not clearly related to this.

The author gives numerous examples of similarities and differences in behaviour and symptoms and discusses them in relation to differences in social and psychological milieux and to the [supposedly] powerful genetic element involved in their causation. *R. H. Cawley*

549. **An Investigation of Dextrocardia with and without Transposition of Abdominal Viscera, with a Report of a Case in One Monozygotic Twin**
C. R. LOWE and T. MCKEOWN. *Annals of Eugenics* [*Ann. Eugen. (Camb.)*] **18**, 267–277, March, 1954. 1 fig., 34 refs.

Among the 293,000 live births in Birmingham during the 15-year period 1937–51, the authors ascertained from hospital and local authority records that 10 children with isolated dextrocardia had been identified. Of these 7 had associated cardiac malformations producing cyanosis; the other 3 were free of other cardiac malformations, but one died early from gross malformation of other viscera, one had mirror-image dextrocardia with transposition of the thoracic viscera and bronchiectasis, and only one was free of any other malformations. None of the 18 sibs of these children was affected. There was no known consanguineous marriage among the parents.

In the same population there were 7 children with dextrocardia together with transposition of the abdominal viscera, while 13 further cases of this abnormality occurring among a total of 95,362 individuals were obtained from the records of the Birmingham Mass Radiography Unit. Of these 20 individuals, only one had any associated heart malformation, and this child had, in addition, no spleen and a universal mesentery; 4 others, all children, had malformations of organs other than the heart, while 3, and possibly 4, had bronchiectasis. Among 51 sibs examined (out of a total of 56), one only was also affected with dextrocardia and situs inversus. In 2 instances the parents were first cousins. Of the sibs, one was a twin and this twin was normal in all respects.

The findings suggest that the inheritance of situs inversus cannot be attributed to a single recessive gene which is fully manifested. The association of the various forms of partial transposition with malformation of the heart, splenic agenesis, and bronchiectasis is confirmed. An additional association, that with persistence of the common mesentery, is established for the first time.
C. O. Carter

550. **Note on the Inheritance of the Duffy Blood-group System and its Possible Interaction with the Rhesus Groups**
J. MOHR. *Annals of Eugenics* [*Ann. Eugen. (Camb.)*] **18**, 318–324, March, 1954. 9 refs.

551. **The Association of Familial Polyposis of the Colon with Multiple Sebaceous Cysts**
M. C. OLDFIELD. *British Journal of Surgery* [*Brit. J. Surg.*] **41**, 534–541, March, 1954. 16 figs., 12 refs.

552. **Congenital Heart Disease. Report on an Unusually High Incidence in One Family**
J. C. JOYCE and S. P. O'TOOLE. *British Medical Journal* [*Brit. med. J.*] **1**, 1241–1242, May 29, 1954. 9 refs.

553. **Pedigree Demonstrating a Sex-linked Recessive Condition Characterized by Draining Ears, Eczematoid Dermatitis and Bloody Diarrhea**
R. A. ALDRICH, A. G. STEINBERG, and D. C. CAMPBELL. *Pediatrics* [*Pediatrics*] **13**, 133–139, Feb., 1954. 3 figs.

Public Health and Industrial Medicine

554. **Some Aspects of Behaviour in Emotionally Disturbed Children**
F. A. HEIMANN and B. W. FOXLEY. *Medical Officer* [*Med. Offr*] **91**, 151–152, April 2, 1954. 1 fig., 2 refs.

The authors consider that manifestations of emotional disharmony in childhood can be generally regarded as a prelude to faulty social relationships, and that a thorough investigation of a difficult child is necessary. Behaviour disorders may be due to constitutional retardation, inferior intelligence, organic defects, or acquired emotional traits; discovery of such cases is largely dependent on the close collaboration of school teachers and health visitors with the medical officer and the child-guidance team, and prophylaxis by means of systematic psychological examinations in schools is held to be more valuable than the study of grossly defective children.

In a study carried out at the Child Guidance Centre, Bournemouth, the scholastic attainment of 133 emotionally disturbed children was found to be below average in 57%, average in 30%, and above average in 13%. The authors point out that investigation should not be limited to " troublesome " children, for of 208 emotionally disturbed children, 44% displayed no disorder of behaviour at school. Further, an examination of 172 children referred for failure in school-work showed that 72% of them had an I.Q. of 90 or above. Emotional disorders are frequently accompanied by neurotic symptoms, and the associated physical signs, such as tic, asthma, stammer, or enuresis, may cause absence from school and thus accentuate the child's backwardness.

F. T. H. Wood

555. **A Note on the Usefulness of Psychiatric Clinics for Pre-school Children**
H. GILLESPIE. *Medical Officer* [*Med. Offr*] **91**, 152–153, April 2, 1954.

The author, working at a special Maternity and Child Welfare Clinic for pre-school children and a Child Guidance Clinic for older children in London, has analysed the reasons for referring children to these two centres in order to discover whether both clinics were dealing largely with the same type of problem. To this end, 100 cases were selected at random from the records of each clinic, and the presenting symptoms in the pre-school cases and comparable symptoms in the older children were noted. Only 10 of the 100 older children failed to present at least one of the characteristic symptoms of the pre-school children, suggesting that the two clinics were in fact dealing with the same type of child.

The results of treatment at the pre-school clinic are reported as encouraging, disappearance of symptoms being obtained in 68% of cases; the failures were largely due to the inability of the parents to cooperate, or to failure to attend for regular interview. A table presenting the result of the investigation shows that behaviour difficulties such as disobedience, tantrums, restlessness, and aggressiveness figured highest in both groups, with emotional disorders such as fears, timidity, overdependence, or unhappiness ranking next in frequency.

F. T. H. Wood

EPIDEMIOLOGY AND IMMUNIZATION

556. **An Outbreak of Food-poisoning due to *Cl. Welchii***
A. BECK, A. W. H. FOXELL, and W. C. TURNER. *British Medical Journal* [*Brit. med. J.*] **1**, 686–687, March 20, 1954. 3 refs.

The authors describe a mild outbreak in a London hospital of food-poisoning due to *Clostridium welchii*. This type of food-poisoning has recently received more attention. As the causative organism is a heat-resistant anaerobe it may escape detection by the routine tests for intestinal pathogens; the illness, a pure lower-bowel affection, follows a mild and short course and is not usually accompanied by the vomiting, pyrexia, and headache which are seen in food-poisoning due to staphylococci or *Salmonella*. In the outbreak described, 39 patients and 5 members of the staff were affected out of 360 at risk, distributed amongst 7 wards of the hospital. Illness set in 8 to 16 hours after a meal of roast pork which had been cooked the day before, open-cooled for 3 to 4 hours before being placed in the refrigerator, sliced and covered with hot gravy the next morning, and transported to the wards in closed hot trolleys.

Cl. welchii was grown from the faeces of 18 out of 40 patients; the resulting, almost pure, cultures gave a positive Nagler reaction [turbidity in human blood serum when *Cl. welchii* toxin is added] and this reaction could be suppressed by Type-A antitoxin. The organism was also isolated from a remnant of the roast pork and recovered also from 3 out of 12 samples of raw pork obtained from the same kitchen refrigerator in which the roast pork had been stored. None of the kitchen staff was found to be excreting the organism. Cultures from the roast pork and from 6 out of 17 specimens of stool were of identical serological type.

The cause of the outbreak is believed to have been the survival of spores of *Cl. welchii* in the centre of the joint which had resisted the heat of cooking. *J. Cauchi*

557. **Does Influenza Spread within the Household?**
R. E. H. SIMPSON and I. SUTHERLAND. *Lancet* [*Lancet*] **1**, 721–726, April 3, 1954. 11 refs.

In this study of the epidemiology of influenza, the authors examined the pattern of the disease in households in and around Cirencester, Gloucestershire, during the influenza epidemic of 1951. Close observation was maintained on 100 households in which at least one case

of influenza was known to have occurred. The households consisted of 385 individuals, including the 100 first affected, and 223 (78%) of the remaining 285 persons subsequently developed influenza within 50 days, 2 women and one man, all aged over 75, dying of the disease.

Details of the sex and age of the patients, size of household, number of subsequent cases, and the interval between cases are shown in tables, and are statistically analysed and discussed. From this information it appears that influenza attacks males and females, old and young, indiscriminately. The attack rate among those exposed to the first case in the household was 90% for households of 2 persons, fell to a minimum of 71% for households of 4, and thereafter rose with the increasing number in the household. Within each household, cases of influenza tended to occur at the same stage of the epidemic, but no evidence could be found of any fixed interval between successive cases of the disease within the same household.

The experience in these households with influenza was analysed and compared with that in an epidemic of measles. This showed clear evidence of direct person-to-person transmission of measles, but in the influenza epidemic only the distribution of multiple attacks in households with 4 or 5 members conformed at all with what was to be expected from this mode of transmission.

The authors conclude that the problem of whether or not influenza epidemics depend on the mechanism of direct spread from person to person could not be settled with the data at their disposal, and suggest that it would be profitable in a future epidemic to make a larger study, collecting information from households selected at random for comparison with that from households selected because they have at least one case of influenza.

Benjamin Schwartz

558. **Primary Response of Children to Glycerinated or Dried Smallpox Vaccines of Calf Lymph or Chick Embryo Origin**

V. J. Cabasso, R. F. Korns, I. F. Moore, and H. R. Cox. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 194–205, Feb., 1954. 3 figs., 16 refs.

In this study, carried out under the auspices of the Bureau of Epidemiology, New York State Department of Health, Albany, the authors vaccinated 104 children with 4 different types of smallpox vaccine derived from either calf lymph or chick-embryo cultures (fifth passage) and prepared in either the glycerinated or dried state. Typical primary " takes " were obtained on 103 of the 104 children. The time of appearance of the early papule, as well as the evolution of the takes, was similar in all cases, and no prolongation was observed in the time in which the area of erythema reached its largest size on children given the chick-embryo preparation. This was equally true for children who were vaccinated on one or both arms. The experiment was fully controlled and the results objectively assessed.

It is pointed out that vaccine of chick-embryo origin gives as good results as calf-lymph vaccine, is much quicker and easier to prepare (at a smaller cost), and also that in it the control of bacterial contaminants is easy, whereas in calf vaccine it is almost impossible. Full details are given for the preparation of the 4 types of vaccine used.

[This is an excellent study and the conclusions appear to be valid. It may well be that vaccine of chick-embryo origin should replace the traditional calf lymph for routine vaccination procedures.] *J. Lorber*

INDUSTRIAL MEDICINE

559. **A Method of Relating the Incidence of Pneumoconiosis to Airborne Dust Exposure**

S. A. Roach. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 220–226, Oct., 1953. 2 figs., 18 refs.

Attempts to relate the incidence of pneumoconiosis to the average dust concentration in the environmental air and length of exposure in various industries in the past are reviewed. In general it has been found that the incidence of the disease increased proportionately with both concentration and length of exposure, but difficulties arise in such studies when only the men who survive in employment are studied, since those worst affected will have left the industry. Moreover, there are many possible sources of error in assessing dust exposure and in the *x*-ray diagnosis and assessment of the severity of the disease.

A method of expressing the total dust exposure of a worker as a single figure is described, and the construction of a curve relating the proportion of men with pneumoconiosis to their dust exposure (" exposure-response " curve) is explained with reference to data obtained at a colliery in England. A rough estimate of the average dust concentration (in particles per ml.) for each year over a period of 14 years was arrived at, from which the average concentration over the whole period of exposure was calculated for each man with an uncomplicated occupational history. This average figure multiplied by the number of years' exposure gave the estimated total dust exposure of each man in " particle-years per ml.". The proportion of men with simple pneumoconiosis having been ascertained radiologically, the exposure—response curve was given by the regression of this proportion on the total dust exposure. The method is identical with that used in biological assay, the position of the curve indicating the potency of the material and the slope being a measure of variation in individual tolerance and errors of measurement.

The construction of such a curve provides an estimate of the pneumoconiosis risk in terms of total dust exposure, and in using it in the prevention of the disease it is first necessary to decide how much pneumoconiosis is to be tolerated in the works concerned. Control may then be secured either by reducing dust concentration or by limitation of exposure time, which might be achieved by establishing an upper age-limit for dusty work. Methods of using exposure-response curves for a comparison of the effect of different airborne dusts are discussed, and it is pointed out that for this purpose standardization of

radiographic and film-classification techniques, as well as of methods of dust sampling and evaluation of the samples would be essential. *L. W. Hale*

560. **The Nature of the Variability of Dust Concentrations at the Coal Face**
P. D. OLDHAM. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 227–234, Oct., 1953. 6 figs., 12 refs.

Dust samples taken with the thermal precipitator at the coalface by the [M.R.C.] Pneumoconiosis Research Unit are analysed to show the kind of variation in dust concentration that is experienced. Although the variability is high, the general run of samples suggests that the range of concentrations is considerably dependent on the average level, and agrees quite well with the assumption of a lognormal distribution of concentrations with an almost constant proportional standard deviation. In consequence the accuracy to be expected in estimating mean concentrations from numbers of thermal precipitator samples can be specified in advance. The 95% fiducial limits of the mean of 10 such samples are 73% to 137%, a range equal to 64% of the calculated mean. Even 50 samples only reduce this range to 23%.

The necessity is pointed out of automatic sampling instruments, which alone can sample inexpensively for sufficiently long to reduce this sampling error, and which are demanded also from consideration of the aetiology and rate of appearance of pneumoconiosis.

On the assumption that " approved conditions " are such that 90% of dust concentrations during a shift are less than 850 particles per ml., it is deduced that this limit is equivalent to an average concentration of between 500 and 600 particles per ml. throughout the working shift.—[Author's summary.]

561. **The Importance of the Time Factor in the Measurement of Dust Exposure**
B. M. WRIGHT. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 235–240, Oct., 1953. 35 refs.

An attempt is made in this paper to estimate the relative importance of dust concentration and duration of exposure in the production of pneumoconiosis. The natural assumption would seem to be that concentration and time are equally important, the amount of dust retained in the lungs being proportional to the product of the two, and this " average " hypothesis has been adopted by all workers who have tried to correlate exposure to dust with incidence of disease, a reasonable correlation having consistently been found. There is a widespread belief among mine-workers, however, that high concentrations of dust may be disproportionately more harmful than lower concentrations; if this is true, periodic " dust-floods " in any process must be detected, and average concentration figures over a period would not provide an adequate basis for the calculation of risk. This is called the " peak " hypothesis.

These hypotheses are discussed in the light of what is known of the mechanism of dust inhalation and retention. It is stated that the rate of accumulation of dust in the lungs is directly proportional to the concentration of respirable dust in the air. There appears to be no mechanism by which an increase in dust concentration could cause a disproportionate increase in the rate of dust inhalation, and experimental work has repeatedly shown that the rate of phagocytosis of dust particles (provided they are not highly toxic) is always equal to the rate of deposition in the alveoli even when very high dust concentrations are inhaled, so that the rate of retention in the lungs is unlikely to be increased by an increase in concentration. Certain considerations which have tended to make the " peak " hypothesis popular, particularly among engineers and non-medical observers, are mentioned and their fallacies pointed out, and it is concluded that this hypothesis is ill-founded and unsupported by evidence.

Finally the author discusses the practical implications of acceptance of the " average " hypothesis in regard to techniques of dust sampling and suppression.

L. W. Hale

562. **Comparison of Different Types of *X*-ray Films for Case Finding and Diagnosis of Silicosis**
D. O. SHIELS and D. L. G. THOMAS. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 200–204, Feb. 6, 1954. 4 figs., 1 ref.

In an investigation undertaken by the Victoria State Department of Health, Australia, 21 healthy men and 46 men suffering from pneumoconiosis, with or without tuberculosis, were radiographed on 35-mm. and 70-mm. film, and the same subjects, together with 5 more patients with pneumoconiosis, on full-size screened and unscreened films. All the sets of films were read independently by 5 radiologists and one silicosis expert. The majority verdict of these 6 generally agreed with that of the medical officer in charge of the case, which was taken as the " correct " diagnosis.

Considerable differences of opinion were noted. On the whole the errors were greatest with 35-mm., intermediate with 70-mm., and least with the full-size films. One observer [presumably the silicosis expert] scored equally well (91 to 98% correct) with all techniques. Despite their findings, the authors conclude that mass miniature radiography may be used for screening an industrial population for pneumoconiosis, since advanced changes will be detected by any technique and in the absence of such changes there can be no serious hazard.

[No details are given of the severity of the pneumoconiosis in the patients examined, but since all had originally been detected by mass radiography it is not surprising that most of them were again diagnosed in this trial. Indeed the fact that a third or more of them were missed by some observers might be thought to contradict the authors' conclusions, which are in fact argued *a priori* without reference to their own findings. There are many curious omissions, not least of which is the absence of any reference to false positive readings in the tables, though these must have occurred.]

C. M. Fletcher

563. **The Threshold of Age**
J. M. MACKINTOSH. *Lancet* [*Lancet*] **1**, 991–994, May 15, 1954.

Forensic Medicine and Toxicology

564. **The Urinary Excretion of Total 17-Ketosteroids in Sexual Delinquents.** (La escrezione urinaria dei 17-chetosteroidi totali nei delinquenti sessuali)
G. GUARESCHI, G. VIDONI, and G. BINI. *Minerva medicolegale* [*Minerva med. leg.* (*Torino*)] **72**, 313–319, Nov.–Dec., 1953. 21 refs.

The urinary excretion of total 17-ketosteroids was examined in 28 male subjects convicted of sexual offences. The method employed was that recommended by the International Congress of Clinical Endocrinology (*Lancet*, 1951, **2**, 585). Two 24-hour specimens of urine were examined, and a third if the first two values differed by more than 3 mg. Normal values obtained by this method in a previous investigation ranged from 6 to 25 mg. in men from 18 to 50 years of age, with variations of 10 to 20 mg.

The first group consisted of 9 men aged 21 to 71 years (mean 40·6) who had committed or attempted rape; the 17-ketosteroid excretion of 2 of these (one being the man of 71) was over 30 mg. and of one was 27 mg. Psychiatric examination showed 8 of the 9 to be apparently normal; the 17-ketosteroid excretion of the remaining one, who was mentally defective, was 5·9 mg. The second group consisted of 7 men aged 20 to 72 (mean 43·3) convicted of exhibitionism, 4 of whom had high normal 17-ketosteroid excretion values (20 to 22 mg.). The third group consisted of 12 men aged 19 to 61 (mean 41·2) convicted of homosexual offences; the 17-ketosteroid excretion of one was over 30 mg., and of 6 others was in the high normal range (19 to 25 mg.).

These findings are taken to indicate that hormonal influences may be a factor in the causation of some sex offences. *V. C. Medvei*

565. **Aspiration of Vomitus by Victims of Road Accidents.** (Die Aspiration bei Opfern des Strassenverkehrs)
E. LÄUPPI. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **84**, 335–338, March 20, 1954. 5 refs.

The author, writing from the Institute of Forensic Medicine, University of Zürich, reviews the findings in 300 necropsies on victims of road accidents who died within 48 hours of injury. In 157 cases (52%) he found evidence of aspiration of blood or vomit. Analysing this over-all figure, he concludes that in 36 cases (12%) the aspiration was of a minor degree and merely coincidental, other damage to vital organs being incompatible with life. In a further 78 cases (26%) the aspiration was of a major degree and would certainly by itself have caused the death of the victim; as other findings, however, such as epidural and subdural haematomata, cerebral lesions, fractures with fat emboli, loss of blood, and shock were of such a degree that death could equally well be attributed to either cause, the author regards aspiration in this group as a "competing" cause of death. In the last group of 43 cases (14%), aspiration some time after the accident was considered to be the sole cause of death, the injuries sustained in the accident being of a minor character only.

In all groups aspiration occurred most frequently among pedestrians, cyclists, and motor-cyclists, the occupants of motor-cars being apparently buffered to some extent against injuries to the pharynx and skull by the metal body of their vehicle. The author stresses the danger caused by the insidious oozing of blood from the nasopharynx in concussed and unconscious patients transported in the supine position, and recommends a publicity campaign urging practitioners, first-aid personnel, and laymen to ensure that unconscious patients are transported either in the prone position or lying on their side. *R. Salm*

566. **The Specificity of the Löns Serological Paternity Test.** (Zur Frage der Spezifität des Serologischen Vaterschaftsnachweises nach Löns)
J. PÜSCHEL, U. LÖNS, and M. FLOREN. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **139**, 27–37, 1954. 6 refs.

The authors claim that the Löns serological test of paternity is highly accurate and specific, supporting their contention with details of a series of 60 cases in which the facts were proved or known and in all of which the Löns test gave the correct result. A number of faults in technique are now believed to have been responsible for previous unreliable results. *G. F. Walker*

567. **Mechanisms of Toxicity of Some Iron Preparations**
J. A. NISSIM. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **9**, 103–105, March, 1954. 3 refs.

568. **Toxic Reactions after Intravenous Saccharated Iron Oxide in Man. Suggestions for Improved Preparations**
J. A. NISSIM. *British Medical Journal* [*Brit. med. J.*] **1**, 352–356, Feb. 13, 1954. 1 fig., 36 refs.

Experiments on animals have shown that the observed toxic effects of intravenous saccharated iron oxide are associated with precipitation. In the mouse and rabbit at a threshold dose of about 45 mg. Fe per kg. body weight precipitation of fine particles of the compound occurs gradually. For this reason toxic effects are noted only after an interval. At a threshold of about 180 mg. Fe per kg. in the rabbit immediate (though partial) precipitation occurs, with multiple embolism.

In man, toxic reactions to the drug given intravenously are of two types, early and late. The early reactions include pain in various parts of the body, symptoms suggestive of sympathetic or parasympathetic stimulation, and symptoms of circulatory collapse. Late reactions include dizziness and weakness, pyrexia and rigors,

generalized urticaria or papular rash, pain, and collapse with a grey colour, tachycardia, loss of pulse, and a subnormal temperature. Early reactions appear within 10 minutes of the injection of relatively small doses in up to 10% of cases. There is evidence that these reactions are less common when highly purified sucrose is used in the preparation of the drug and when the interval between preparation and use is short. Only 13 cases of late reaction have been reported in Great Britain, and their frequency evidently depends on the dosage used, which was less than 300 mg. Fe in only 3 of the 13 cases.

It seems reasonable to suppose that the late reactions in man are due to precipitation, since they are less common with samples possessing a high LD_{50} for animals and a high threshold of precipitation, and they are of a similar nature to those following injections of colloidal ferric hydroxide, which is known to precipitate in the plasma. Early reactions in man are probably due to other factors, such as individual hypersensitivity to impurities in commercial (*B.P.*) sucrose. Support for the view that the two types of reaction to intravenous saccharated iron oxide are of different origin has been provided by Ramsey (*Brit. med. J.*, 1950, **1**, 1109; *Abstracts of World Medicine*, 1950, **8**, 510) who injected doses of 300 to 900 mg. Fe into 11 patients. Delayed reactions, which are extremely rare with doses under 300 mg., occurred following 9 of the 16 injections, whereas early reactions occurred in only 3 cases, which is a frequency not much higher than that obtained with smaller doses, while 2 of the 3 patients developed late reactions after a symptom-free period of several hours. One fatal reaction has been described in the 6 years since saccharated iron oxide was first introduced for intravenous administration. The reaction was probably of the early type, and no emboli were found at necropsy. It is likely that the cause of death in this case was cardiac ischaemia, especially as there was post-mortem evidence of calcification of both coronaries with complete occlusion of the right artery, and the need for particular care in patients with arteriosclerosis is stressed.

The author suggests that the incidence of reactions to this valuable preparation might be reduced by using only sucrose of high standard in its manufacture, and by keeping the compound in powder form in ampoules for solution immediately before use. Separation of impurities by dialysis and fractional ultrafiltration to remove the larger colloidal particles are other possible measures. *Robert Hodgkinson*

569. **Experimental and Clinical Aspects of the Acute Toxicology of Isoniazid.** (Rilievi sperimentali e clinici di tossicologia acuta della idrazide dell'acido isonicotinico)
M. Aiazzi Mancini. *Minerva medica* [*Minerva med. (Torino)*] **1**, 529–530, Feb. 24, 1954. 15 refs.

The toxicology of isoniazid is important because faulty administration of this increasingly-used drug may be dangerous, and it has been used in some instances to commit suicide. It is a convulsant, perhaps either through the action of its breakdown products or by its direct diffusion into the cerebrospinal fluid, in which there may be a critical threshold concentration. Results vary in experimental animals; the minimum convulsant dose in the dog is 40 to 50 mg. per kg. body weight, the minimal lethal dose, given intravenously, being 70 to 80 mg., while in the monkey double these doses are required. Convulsions begin after a time varying inversely with the dose, the minimum being 15 minutes, the dog dying in status epilepticus after 2 to 4 hours of increasingly frequent attacks. Symptoms do not vary in nature and mode of onset with different routes of administration, but the risk with lumbar infusion is less than that with cisternal infusion, since the blood concentration is raised more rapidly in the latter. A cisternal dose of 4 mg. per kg. body weight is fatal in the dog, while the monkey tolerates twice that amount.

In the human subject errors of administration have similar results. A woman weighing 55 kg. who received 5·5 g. of isoniazid developed fits within 30 minutes and required deep barbiturate sedation lasting 24 hours. In a case of suicide by isoniazid, similar symptoms developed. When renal function is intact, human sensitivity is probably intermediate between that of the dog and monkey, the threshold concentrations in the cerebrospinal fluid and in the plasma being of the order of 30 μg. per 100 ml. in the dog and 60 μg. in the monkey. In practice, treatment is by the administration of barbiturates, since glutamic acid, recently suggested as being of value, is not likely to be immediately available. When convulsions are present a rapidly acting barbiturate such as thiopentone given intravenously is imperative, and if the dose of the toxic agent is large or unknown, a long-acting barbiturate such as phenobarbitone should also be given intramuscularly, the dose of thiopentone being 10 or 20 mg. per kg. body weight and of phenobarbitone 80 or 100 mg. per kg. divided into 3 or 4 doses so as to maintain coma while the levels of isoniazid in the blood and cerebrospinal fluid are above the convulsive threshold. *W. A. Bourne*

570. **The Acid–Base Disturbance in Salicylate Intoxication**
R. B. Singer. *Medicine* [*Medicine (Baltimore)*] **33**, 1–13, Feb., 1954. 5 figs., 31 refs.

From a review of 26 cases in the literature and 2 personal cases seen at the Hospital of the University of Pennsylvania, Philadelphia, the author discusses the acid–base disturbance in salicylate intoxication. Changes in the acid–base balance occurring in these cases (a total of 83 observations) were analysed and compared by means of the nomogram of Singer and Hastings with the changes encountered in cases of respiratory alkalosis and metabolic acidosis. This showed that the disturbance in salicylate intoxication is a mixed one, consisting in an initial phase of respiratory alkalosis followed by a metabolic acidosis, especially in infants. The hyperventilation and respiratory alkalosis are due to a specific pharmacological action of the salicylate. The mechanism of the metabolic acidosis is not known. The author emphasizes that it is necessary to estimate both the plasma CO_2 concentration and the *p*H for correct treatment of these cases. *H. B. Stoner*

Anaesthetics

571. **Bleeding from Cut Skin and Subcutaneous Tissue Surfaces during Cyclopropane Anaesthesia**
G. McLoughlin. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **26**, 84–99, March, 1954. 2 figs., 40 refs.

In an investigation carried out at the United Liverpool Hospitals the blood loss from a standard skin puncture in the various planes of Stage-3 cyclopropane anaesthesia was compared with that occurring under ether anaesthesia. The skin on the dorsal surface of the finger was punctured with an automatic lancet, a cuff at 40 mm. Hg being applied to the upper arm, and the blood shed collected on filter paper, the area of bloodstaining being measured in square centimetres. After premedication with atropine and morphine, anaesthesia was induced with thiopentone sodium, the maximum dose being 0·5 g. In 100 cases cyclopropane was used to maintain anaesthesia, and in 50 cases ether was used. Estimations of blood loss were made in each case before and during anaesthesia, together with recordings of the blood pressure, pulse rate, and depth of anaesthesia, and the ratio of the blood loss in each plane to the preoperative blood loss was calculated.

In the group given cyclopropane the average preoperative blood loss was 1·74 sq. cm.; in Plane I the average blood-loss ratio was 8·3, in Plane II 4·0, and in Plane III to IV 2·16 when respiration was aided and 9·37 when respiratory depression was deliberately allowed to occur. After hyperventilation the mean blood-loss ratio was reduced by 30·6% in Plane II and 80·2% in Plane III. In the group given ether the average preoperative blood loss was 1·92 sq. cm. The mean blood-loss ratio in Plane I was not measured, in Plane II it was 2·61, and in Plane III 2·64.

Thus it appears that with cyclopropane peripheral bleeding is increased in inverse proportion to the depth of anaesthesia in Planes I and II, blood loss in Planes III to IV being markedly reduced by the prevention of respiratory acidosis. Comparison of the mean blood-loss ratios in Plane II shows that cyclopropane produces approximately 1½ times as much bleeding as ether.

D. J. Pearce

572. **Hypothermia in Cardiac Surgery**
D. F. Downing, B. A. Cookson, K. K. Keown, and C. P. Bailey. *Journal of Pediatrics* [*J. Pediat.*] **44**, 134–144, Feb., 1954. 18 refs.

At Hahnemann Medical College and the Bailey Thoracic Clinic, Philadelphia, the authors repeated some of Bigelow's experiments on the effects of hypothermia in dogs in order to try to solve some of the problems encountered. After a preliminary series of experiments to acquire familiarity with the technique, 27 dogs were cooled to 24° to 26° C. (75·2° to 78·8° F.), the venae cavae being occluded for 12 minutes. The right atrial wall was incised and explored under direct vision in 8 cases, and the right ventricle in 9, 23 (85·1%) of the dogs surviving. The first 11 dogs received atropine and morphine followed by thiopentone (30 mg. per kg. body weight) intravenously. They were cooled in a commercial beverage cooler, respiration being controlled by means of an automatic respirator supplying pure oxygen. After thoracotomy, 10 ml. of 1% procaine solution was injected into the pericardium, the venae cavae were occluded by clamps, piperoxan (" benodaine ") 0·8 mg. per kg. was injected into the right ventricle, and after 5 minutes the inferior vena cava was partly released; the injection was repeated after another 5 minutes and the vessel completely released. After insertion of a drainage tube, the chest was closed, penicillin, thiamine chloride, and 50% glucose being given. The other 16 dogs were similarly prepared, but in addition digitoxin was given at the beginning of, and " vasoxyl " during, the operation; more atropine was given if there was bradycardia, and thiamine chloride and 50% glucose before and after cooling and immediately preoperatively. In this group the piperoxan was withheld until it was ascertained that there was no sign of heart block (one death having occurred from this in the first group). Piperoxan was given on the assumption that ventricular fibrillation may be due to the sudden release of adrenaline which has accumulated while the venae cavae are clamped. In another series of experiments " WIN 2173 " (an *iso*quinoline derivative) was used in 5 cases to counteract the severe bradycardia of profound hypothermia, with encouraging, but not conclusive, results. In the next series 10 dogs were cooled to 26° C.; right atriotomy was performed, a defect was created in the interatrial septum, and the left heart was explored digitally, the heart then being resutured. An arterial transfusion at a pressure of 70 mm. Hg was given to prevent air embolism, a suspension of erythrocytes in Ringer–gelatin solution being used. Finally, 3 dogs were cooled to 21° to 24° C. (69·8° to 75·2° F.) and the heart and lungs were removed and replaced by those from donors; one animal survived for 6 hours, with return of reflexes, spontaneous respiration, and a normal electrocardiogram (ECG). It was concluded from these animal experiments that cooling to 26° C. (78·8° F.) allows the circulation to be interrupted for 12 minutes with relatively little effect. Arterial transfusion seemed to be helpful.

The technique has been used by the authors for intracardiac operation on 16 human subjects aged 10 days to 33 years, of both sexes; 2 were cooled in a " deep-freeze " unit, but cooling was too slow so a cooling blanket was used for the remainder, iced water being pumped through the coils. After placing the patient on the blanket, an endotracheal tube was passed, enough thiopentone given to produce narcosis, and a slow drip infusion of 0·2% procaine in 5% glucose solution started, 100% oxygen being given by inhalation from the start; a rectal thermocouple was introduced, electrocardiographic leads attached, the blanket wrapped round the patient, and cooling started. When the temperature was a few degrees

above that required the blanket was opened, a further fall of 2° F. then occurring. The temperature was then controlled by warming or cooling the water flowing through the blanket. Shivering occurred early (except in infants) and was controlled by giving more thiopentone. Spontaneous respiration ceased at about 28° C. (82·4° F.), and returned at the same temperature on recovery. The ECG showed prolongation of the R–R, P–R, and S–T intervals; sinus rhythm was usual. The blood pressure fell gradually as the temperature fell, and the pulse slowed after an initial rise. Rewarming (by passing warm water through the blanket) was carried out rapidly up to 28° C. (82·4° F.) and then more slowly; at 31° to 32° C. (83·8° to 87·6° F.) the patient was returned to bed. Of the 16 patients operated on for atrial and ventricular septal defects (3), Fallot's tetralogy (4), transposition of great vessels (4), pulmonary stenosis (3), and mitral and aortic incompetence (1 each), 11 died, 4 of whom were adults and the remainder extremely poor risks.

The tentative conclusion is drawn that hypothermia is indicated in severely cyanotic and disabled infants undergoing intracardiac surgery, the optimum temperature being 23·3° to 26·1° C. (74° to 79° F.). It is unnecessary in the presence of a non-cyanotic lesion, where the circulation need not be interrupted, and is contraindicated for patients over the age of 10 years.

D. D. C. Howat

573. **The Anaesthetic Management of Patients with Poliomyelitis and Respiratory Paralysis**

E. W. Anderson and B. Ibsen. *British Medical Journal* [*Brit. med. J.*] **1**, 786–788, April 3, 1954. 2 refs.

Experience in the 1952–3 epidemic of poliomyelitis in Denmark is recorded, 3,722 cases being treated at Blegdams Hospital, Copenhagen, over a period of 8 months. Of these, 349 had respiratory or swallowing difficulties, or both. In the first 2 months, 27 out of the 31 patients with respiratory paralysis died. By this time the epidemic had assumed vast proportions, necessitating a rapid and wholesale reorganization. In the light of initial experience the following special measures were adopted. (1) Transport. It soon became clear that acute cases did not tolerate transport well, and tracheotomy had often to be performed in the ambulance on the way to hospital. It was decided, therefore, to provide an emergency team consisting of an otologist, an anaesthetist, and a nurse, who were equipped for performing tracheotomy in the home before removal of the patient. This measure brought gratifying results and a dramatic lowering of mortality. (2) For patients with respiratory or pharyngeal paralysis and for those with such rapidly ascending paralysis that difficulties could be expected, special observation wards were prepared, where the main aim was to correlate clinical and laboratory findings so as to establish what specific treatment, such as postural drainage, mechanical respiration, or tracheotomy, with or without manual ventilation, was required.

(3) Tracheotomy. The main indications for this procedure were a blocked airway or inadequate or deficient ventilation. The technique changed in the light of experience. At first it was performed under local analgesia, but the mortality was alarmingly high, largely due to inhalation of gastric contents or to deficiency of ventilation necessarily imposed by the operation. Thereafter, general anaesthesia was employed and gave immediately improved results. A stomach tube was passed and usually retained afterwards for drainage and feeding. Tracheal intubation was performed under cyclopropane, using a to-and-fro CO_2 absorber, by the semi-open method; difficulties were often encountered here due to secretions and to the light degree of anaesthesia preferred. After inflation of the cuff, tracheotomy was performed at leisure, the high approach being chosen to reduce the risk of entry of the tip of the tube into the right main bronchus. The indwelling tube, however, resulted in a high rate of complications. A tank respirator was found unsuitable for this operation. Surgical complications were rare, a fact attributed to the employment of general anaesthesia. The immediate postoperative period was often critical, and pulmonary oedema due to respiratory obstruction—especially inhalation of gastric contents—was the main complication. Assisted respiration for the first few hours was found an effective measure and slight positive pressure was added if oedema was suspected; the usual precaution of not overloading the circulation with fluids was observed, and venesection was performed if signs of pulmonary oedema persisted. (4) Ventilation. Manual ventilation was found preferable to mechanical respirators as a routine, because access to the patient for nursing, drainage, and change of posture were so much easier. A mixture of 50% nitrogen and oxygen was supplied to the patient through a semi-closed to-and-fro absorber, keeping the reservoir bag half-filled. The flow was 5 to 6 litres per minute and manual inflation was performed at the rate of 16 to 25 times per minute for adults and 20 to 30 times for children. Emphasis is placed on rapidity of the inspiratory phase and on the need for ensuring that the pressure in the airways be allowed to fall to zero during expiration. At first, when pure oxygen was used, patients complained of a substernal burning sensation and were thought to be suffering from oxygen poisoning; the substitution of the oxygen–nitrogen mixture eradicated this symptom. The semi-closed method provided the buffer effect of the canister and bag as a safeguard in the absence of fully trained personnel. Suction was performed as a routine with Nélaton and Tiemann catheters but, if ineffective, a large-bore tube was passed directly into the trachea after extubation. Bronchoscopy was reserved for cases with persistent atelectasis, but resort to this procedure became less frequent with experience. (5) Secondary shock was of vital importance and full measures were instituted to prevent or counteract it.

The authors append a helpful list of the equipment which they found necessary to have on hand for each patient as a routine.

[This review of magnificent organization in the face of mass calamity will undoubtedly be of the greatest help in the future, and at the present must command the respect and admiration of all. The more detailed account promised in the future will be awaited with interest.] *Michael Kerr*

Radiology

574. **An Investigation into the Haemodynamics of Angiocardiography and Aortography in Experimental Animals.** (Tierexperimentelle Untersuchungen zur Hämodynamik der Angiokardiographien und Aortographien)
G. GRABNER, F. KAINDL, and W. WEISSEL. *Wiener Zeitschrift für innere Medizin und ihre Grenzgebiete* [*Wien. Z. inn. Med.*] **35**, 1–9, Jan., 1954. 2 figs., 7 refs.

To elucidate the cause of the occasional ill effects of aortography and angiocardiography, animal experiments were performed at the Second University Medical Clinic in Vienna. The circulatory changes sometimes observed might be due either to the rapid injection of a large volume of fluid or to a toxic effect of the iodine compound used as contrast medium. Hence the haemodynamic and respiratory effects of injecting an indifferent fluid, such as heparinized whole blood or physiological saline, were compared with those of injecting a similar volume of contrast medium by the techniques used in venous angiocardiography and direct aortography in dogs anaesthetized with morphine and chloral. Angiocardiography was performed by cannulating the right axillary vein, 8 animals receiving the contrast medium and 16 the indifferent fluid. Contrast medium caused bradycardia, whereas the heart rate was little changed by the indifferent fluids. The auricular, pulmonary arterial, and aortic pressures rose initially with either injection, but in the animals given contrast medium there was a secondary rise of pressure in the pulmonary artery and at the same time a marked fall in aortic pressure, which was not restored to normal for many minutes. Only the contrast medium markedly affected respiration, causing tachypnoea followed by shallow, slow respiration. In half the animals there was initial apnoea for 10 to 15 seconds.

Aortography was performed by catheterization from the right carotid artery. Standardization of experimental conditions was difficult, the positions of the instillation and measuring catheters varying from case to case. Four dogs received saline and 4 the iodine compound. Again the latter caused bradycardia (which was less marked in one dog which had undergone bilateral cervical vagotomy) and, after an initial rise in both pulmonary arterial and aortic pressures, a fall in the latter occurred and a secondary rise in the former. All the animals given intra-aortic injections of contrast medium developed tonic–clonic convulsions after an interval of 8 to 18 minutes and died.

The authors show that the changes observed are not explicable by simple haemodynamic principles alone, nor by invoking Starling's Law of the Heart, and postulate that they are at least partly due to a reflex action of the central nervous system which is elicited even by indifferent fluids, but is more marked when contrast medium is injected. The primary effect is probably on the aortic pressure, the respiratory changes and rise in pulmonary arterial pressure being secondary to the aortic hypotension. *D. Goldman*

575. **The Use of Angiocardiography in the Selection of Patients for Mitral Valvular Surgery**
H. F. ZINSSER and J. JOHNSON. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 1200–1218, Dec., 1953. 12 figs., 6 refs.

Ordinary clinical and radiographic methods of assessing the degree of stenosis present in mitral disease are not always helpful in the selection of cases which might benefit from surgery. The authors have found that valuable information can be obtained by means of angiocardiography about the rate of flow from the left auricle into the ventricle during diastole.

At the Hospital of the University of Pennsylvania, 150 patients with mitral disease were investigated by means of angiocardiography, the technique followed being that of Robb and Steinberg, but all films were taken in the left oblique position, nearly lateral. In 2 cases of pure mitral stenosis the left auricle became densely opacified and remained so for an abnormally long time. Subsequently the left ventricle became visible. Either or both of these chambers might be enlarged, but the authors stress that in evaluating the indications for surgery it is less the size of the auricle than the constant difference between auricle and ventricle which is the significant factor. In 88 cases there was a loud apical systolic murmur which raised the question of mitral insufficiency, but 63 of these showed the angiocardiographic pattern described. Of these, 57 were confirmed at surgery as being predominantly stenotic. Of the other 6 cases, in which the mitral opening seemed adequate, 5 were improved after surgical enlargement of the orifice.

The authors postulate from this experience a type of functional stenosis, revealed by the angiocardiogram, even in the presence of an apparently adequate valve opening. These cases would appear to benefit from cardiac surgery. *A. M. Rackow*

576. **Visualization of Valvular and Myocardial Calcification by Planigraphy**
L. A. SOLOFF, J. ZATUCHNI, and H. FISHER. *Circulation* [*Circulation (N.Y.)*] **9**, 367–370, March, 1954. 4 figs., 5 refs.

577. **The Value of Trans-splenic Splenoportography in Echinococcosis of the Liver.** (Intérêt de la splénoportographie transplénique dans l'échinococcose hépatique)
R. BOURGEON, H. PIETRI, and M. GUNTZ. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **43**, 168–176, Feb., 1954. 7 figs.

See also Tuberculosis, Abstract 362.

History of Medicine

578. **Achievements of Chinese Medicine in the Northern Sung Dynasty (960–1127 A.D.)**
LEE T'AO. *Chinese Medical Journal* [*Chin. med. J.*] **72**, 65–82, Jan.–Feb., 1954. 5 figs., 12 refs.

The Northern Sung dynasty brought peace to a large area of China after fifty years of feudal warfare following the fall of the T'ang dynasty, and initiated a period of technical and commercial development. In the field of medicine, the invention of printing by movable type early in the 11th century made possible a more widespread knowledge of medical ideas, and cultural intercourse with the Moslem empire enhanced the Chinese knowledge of pharmacology.

The new government wielded great power in the medical world. Ancient medical texts were revised and a large number of works on materia medica were compiled on imperial authority. The *Sheng Huei Fang*, a formulary issued about A.D. 992 in 100 volumes, contained 1,670 divisions with 16,834 recipes, and was issued to the provinces as a guide to dispensing. The state monopoly of trade embraced drugs, the first shop for the sale of which was established in 1076.

Little advance was made during this period in theoretical medicine, which had become divorced from practical observation and was noted for its flowery language and mystical thought. In clinical medicine, however, full case records show that considerable progress was made in the recognition of diseases, and, more particularly, in the use of the appropriate drugs. Smallpox, measles, and chicken-pox were differentiated. Improvements were made in the treatment of children's diseases, and the importance of nutrition was recognized, particularly in pregnancy and tuberculosis. Better surgical methods included the use of hot compresses, disinfected needles, and silk packing for wounds. Achievements in pharmacology were the introduction of mineral drugs, the beginnings of organotherapy, and the discovery of new pain-relieving drugs, such as opium from the poppy. Some interest in anatomy was aroused by the systematic application of the ancient sciences of acupuncture and moxa, but in the absence of dissection little progress was made.

Medical organization was controlled by the Hanlin College of Medical Officers, through which all important medical appointments were made. By the end of the dynasty corruption was rampant, and a multitude of sinecure posts were held by persons with no medical training. Education was at first haphazard, but the medical school system which had existed in the previous T'ang dynasty was restored in 1076, when the Imperial Medical College became an independent institution.

Numerous practical achievements, although clogged by mysticism and the adaptation of medicine for state purposes, are presented in this picture of medieval Chinese medicine. *F. M. Sutherland*

579. **Anorexia Nervosa in the Time of Lasègue and Gull.** (L'anorexie mentale au temps de Lasègue et de Gull)
J. DECOURT. *Presse médicale* [*Presse méd.*] **62**, 355–358, March 3, 1954. 2 figs., 15 refs.

The author draws attention to the fact that, since 1914, there has been a tendency to confuse the classic anorexia nervosa of Lasègue and Gull with the pituitary cachexia of Simmonds, which may lead to serious errors in treatment. He therefore reviews the former authors' ideas concerning the disease they described and its treatment, and discusses the problem of priority.

There is no doubt that Lasègue was slightly earlier in the field with a psychological analysis, although the condition had been described as early as 1689 by the English author, Richard Morton, under the name of "nervous atrophy or phthisis". Lasègue's original monograph—*De l'anorexie hystérique*—appeared in April, 1873, and described 8 cases, with full appreciation of their mental origin. The monograph was translated into English and published in the London *Medical Times and Gazette* in September, 1873. Four weeks later, in the same journal, appeared an account of a communication made by Sir William Gull to the Clinical Society on October 24, 1873, stating that Lasègue did not seem to be aware of an address which he had delivered at the meeting of the British Medical Association at Oxford in 1868 in which he described "a form of disease occurring mostly in young women between the ages of 15 and 23 and characterized by extreme emaciation". This condition he had then called "apepsia hysterica", but he now proposed the name of "anorexia nervosa". But in the published version of the address to which Gull refers he mentions "apepsia hysterica" only in passing and neither here nor in any other paper published before October, 1873, was there any account of the disease which would support his claim to priority, although from the excellence of his description given to the Clinical Society it is clear that he was familiar with the condition —indeed he amplified Lasègue's account in a number of ways.

The changes of opinion as to the aetiology of the disease over the years are noted, and also the gradual evolution of treatment by isolation, separation from family influences, and humane but firm psychotherapy, as elaborated by Dejerine in 1911 in his *Manifestations fonctionelles des psychonévroses et leur traitement par la psychothérapie*. It was not until 1914 that Simmonds first described the syndrome of pituitary cachexia, differing radically from anorexia nervosa but often confounded with it. *D. P. McDonald*

580. **Allessandro Manzoni, "Medical Historian". (The Plague of Milan, 1630)**
H. M. GILLES. *Oxford Medical School Gazette* [*Oxford med. Sch. Gaz.*] **6**, 15–19, 1954.

581. **Paul Ehrlich. Born March 14, 1854**
H. DALE. *British Medical Journal* [*Brit. med. J.*] **1**, 659–663, March 20, 1954. 1 fig.

The period of his collaboration with von Behring is chosen as the introductory point for this study of Paul Ehrlich, whose extensive and pioneer work on immunology had largely evolved from Behring's discovery of diphtheria and tetanus antitoxins.

The practical and theoretical significance of Ehrlich's work in this field is extensively discussed as being one of the most important aspects of his research. In addition to this, his work in laying the foundations of modern chemotherapy is traced in some detail. He appears to have had, even in his student days, a great interest in the affinities of different tissues for various dyes and other substances. His use of methylene blue is seen as " one of the principal landmarks in the history of modern therapeutics ", and his discovery of salvarsan (arsphenamine) was an extension of the same principle. This thoughtful appreciation of Ehrlich's significance in the long history of medicine concludes with a brief sketch of his unusual personality. *Calvin P. B. Wells*

582. **Paul Ehrlich—Memories of 1905–7**
C. H. BROWNING. *British Medical Journal* [*Brit. med. J.*] **1**, 664–665, March 20, 1954.

583. **Paul Ehrlich—Some Reminiscences**
M. MARQUARDT. *British Medical Journal* [*Brit. med. J.*] **1**, 665–667, March 20, 1954. 1 fig.

584. **Emil von Behring. Born March 15, 1854**
A. S. MACNALTY. *British Medical Journal* [*Brit. med. J.*] **1**, 668–670, March 20, 1954. 1 fig., 6 refs.

In this paper the author describes the main contributions to medicine made by Emil von Behring. His association with Koch and later with Kitasato led to his discovery of the antitoxins of diphtheria and tetanus. The influence of this work is recorded together with the later toxin–antitoxin modification.

A section of the paper is devoted to Behring's work on the immunity problems of tuberculosis, and some account of the range of his medical interests is briefly given.
Calvin P. B. Wells

585. **Thomas Peacock. A Sketch**
I. PORTER. *St. Thomas's Hospital Gazette* [*St Thom. Hosp. Gaz.*] **52**, 50–56, April, 1954. 9 figs.

Thomas Peacock, the son of a Quaker merchant, was born at York on December 21, 1812. After attending a boarding school at Kendal and serving an apprenticeship of 5 years to John Fothergill, a surgeon of Darlington, he became a student at the newly-founded University College Hospital in London. Here he attended the lectures of John Elliotson and Samuel Cooper and was an assiduous note-taker. He spent some time with Mr. Nasmyth, the eminent dentist, and for one year followed the surgical practice of St. George's Hospital. In 1835 he qualified, becoming a Member of the College of Surgeons and a Licentiate of the Society of Apothecaries, but during the next 2 years ill health obliged him to make two voyages to Ceylon. Before returning to England he studied for a few months in Paris. After holding the post of house surgeon at the Chester Infirmary he went to Edinburgh, where he took his M.D. and was for a time house physician and pathologist at the Royal Infirmary. The experience gained in these two appointments was the basis of his extraordinarily wide knowledge of morbid anatomy. At the age of 32 he returned to London, was admitted a Member of the Royal College of Physicians, and was appointed to the staff of the Aldersgate Street Dispensary and the Royal Free Hospital. He was one of the founders of the dispensary in Liverpool Street which eventually developed into the Victoria Park Hospital for Diseases of the Chest. He became a prolific contributor to medical journals and published separate works entitled *Tables and Weights of Some of the Organs of the Body* (1846), *On Aneurysm of the Coronary Arteries* (1849), and *The Weight and Dimensions of the Heart in Health and Disease* (1858). His magnum opus, however, was the beautifully illustrated book on *Malformations of the Heart* (1858), which remained the standard work on the subject until the publication of Maude Abbott's monograph in 1926. He was appointed Assistant Physician to St. Thomas's Hospital in 1849 and was full Physician from 1862 to 1877. At the Royal College of Physicians he held several offices, including that of Croonian lecturer for 1864. He was a masterly clinician, forever checking his diagnosis in fatal cases by meticulous post-mortem examination. As a writer and lecturer he was conscientious and laboriously accurate, if somewhat dry. He formed a great collection of morbid specimens, many of which he presented to Victoria Park Hospital, St. Thomas's, the Royal College of Surgeons, and the Pathological Society; of this last body he was sometime President and one of its most constant supporters. On May 30, 1882, he was taken ill during a visit to St. Thomas's Hospital and died the same evening in the ward to which he had formerly been physician. *W. J. Bishop*

586. **Thomas Willis and the Oxford Anatomy School.** (Thomas Willis et les anatomistes d'Oxford)
R. M. GARRAUD. *Presse médicale* [*Presse méd.*] **62**, 481–482, March 24, 1954. 4 figs., 2 refs.

The University of Oxford, among its many claims to glory, has counted among its members a distinguished line of anatomists. The names of Harvey, Willis, Lower, and Highmore are familiar to all, but others have also left their imprint in the history of anatomy. Among these were Boyle, Frank Nicholls (1699–1778)—who was a teacher of William Hunter and who indirectly furthered the study of anatomy in the United States, for his personal collection of anatomical specimens was later presented to Harvard Medical School—Alcock (1707–79), Kidd, Acland, Rolleston, and Arthur Thomson.

Undoubtedly the greatest period in anatomical study and teaching at Oxford was the last half of the 17th century. Though Harvey spent the later years of his life there working on embryology, the outstanding teacher of that time was Thomas Willis (1621–75), in whose *Cerebri anatome*, published in 1664, is contained

the description of the arterial circle at the base of the brain which is named after him. The illustrations of this work are by Christopher Wren, and include diagrams showing the circle, the vagus nerve, and the sympathetic chain. A contemporary of Willis was Richard Lower (1631–91), a talented anatomist whose careful dissections of the heart are collected in his *Tractatus de corde* (1669). He was also a brilliant experimental physiologist and proved that the blood, in passing through the lungs, changed its colour by taking some " quality " from its contact with the air. He also performed blood transfusions. Other contemporaries were Robert Boyle (1627–91) who discovered the means of preserving anatomical specimens in alcohol, and Nathaniel Highmore (1613–84) who described and illustrated his discovery of the maxillary sinus in his *Corporis humani disquisitio anatomica* (1651).

Willis, Boyle, Lower, and Highmore were all private teachers and regularly practised the injection of the vessels in their anatomical preparations as an aid to demonstration. Indeed, Lower wrote to Boyle in 1664 commenting that " without syringes anatomy would be as much deficient as physic without laudanum ", and Willis pointed out that the vessels of the brain were seen better and more distinctly if a dark liquid had previously been injected into the carotid arteries. By comparison with these four great anatomists, their contemporaries associated with the chair of medicine who were charged with the teaching of anatomy in the University did not shine with any particular brilliance. *H. P. Tait*

587. **John of Arderne, the Father of British Proctology**
T. McW. Millar. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **47**, 75–84, Feb., 1954. 7 figs., 5 refs.

John of Arderne (1307–90) lived in the century which saw the Black Death (1349) and the greater part of the Hundred Years War. Chaucer was born 20 years later and lived to the end of the century. Though John of Arderne witnessed the fusion of Saxon and French into the English tongue he wrote in the language of the clergy and the savant—Latin. He is believed to have been educated at Montpellier, where he probably came under the influence of Henri de Mondeville (1260–1320) and Guy de Chauliac (1300–68).

He served in France with the Duke of Lancaster and is said to have been at the battle of Crecy (1346). From 1349 (" from the first pestilence ") until 1370 he lived in Newark, where he appeared to have had an extensive practice and probably lived under the patronage of the Duke of Lancaster. At the age of 63, when he moved to London, he began to write his monographs; it is from these that John of Arderne must be judged for there are few references to him in other works. They reveal a cultured person with high ethical principles, a surgeon of originality and competence, and a graphic writer.

John of Arderne wrote a series of monographs which together form a fairly complete system of surgery, its popularity being revealed by the known existence of some 60 manuscript copies. In the section on anorectal conditions he digresses on " The Manere of the Leech ", recommending piety, modesty, studiousness, and the avoidance of cynicism and jealousy. He advises his readers not to promise a cure before the patient has been examined, and when asked how long the cure will take " to state double the expected time ", for " if the cure be speedy the credit is to be given to the patient . . . that he had able flesh to heal ". He broke no new ground here for it was the custom to preface any work with a chapter or two of philosophical and practical observations. He also gives advice on fees: " never less than 100 shillings " for the cure of fistula-in-ano. He was in advance of his time in his recommendations about cleanliness in the treatment of wounds (" Have the leech also clean hands and well shaped nails and cleansed from all blackness and filth "), his principles of wound treatment, and his method of controlling haemorrhage.

John of Arderne can be regarded as the father of British proctology, since he described and practised what is virtually the modern operation for fistula-in-ano. Albucasis (*circa* 1106) taught that complete fistulae were incurable but recommended the use of a cautery and the seton; de Salicet, Lanfranc, and de Mondeville held similar views. As the present author points out, it is sad to reflect that this excellent operation of Arderne was neglected until Percivall Pott (1765) once again recommended the laying open of the tract by incision. John of Arderne advised digital examination of the rectum and the use of a flexible probe in exploring fistulae. He gives, for a medieval author, an unusually detailed description of the operation for fistula. Subsidiary tracks should be laid open if the patient will stand the ordeal, or deferred until another time, though it was recognized that healing might occur if the main track had been dealt with. There is a long dissertation on haemorrhoids, an excellent description of cancer of the rectum, and shorter sections on tenesmus, pruritis ani, and prolapse of the rectum. For many of these conditions he advised numerous remedies, including an ointment containing twelve ingredients, " polypharmacy with a vengence ", for while he was in many ways in advance of his time he was also of his time, paying due heed to the magic of potions and ointments and the influence of the phases of the moon on surgery.

J. G. Bonnin

588. **Neuropsychiatric Patients Reported Cured at St. Bartholomew's Hospital in the Twelfth Century. Selected Cases from the Book of the Foundation of St. Bartholomew's Church in London**
H. A. Wilmer and R. E. Scammon. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **119**, 1–22, Jan., 1954. 2 figs., 11 refs.

589. **The Error of Gustav Passavant**
J. Calnan. *Plastic and Reconstructive Surgery* [*Plast. reconstr. Surg.*] **13**, 275–289, April, 1954. 10 figs., 16 refs.

590. **Lead and Lead Poisoning in Early America—Clinical Lead Poisoning in the Colonies**
C. P. McCord. *Industrial Medicine and Surgery* [*Industr. Med. Surg.*] **23**, 120–125, March, 1954.